JAN

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U.S. DEPARTMENT OF COMMERCE
Patent and Trademark Office

SEARCH REQUEST FORM

Requestor's Name: FONDA 7:970 Serial Number: 09/712364

Date: 6-4-01 Phone: 308-1620 Art Unit: 1623

Room NO Box: CM1 8B19

Search Topic:
Please write a detailed statement of search topic. Describe specifically as possible the subject matter to be searched. Define any terms that may have a special meaning. Give examples or relevent citations, authors, keywords, etc., if known. For sequences, please attach a copy of the sequence. You may include a copy of the broadest and/or most relevent claim(s).

bib, assignee data attached.

please search attached. claims 21-25.
See my notes on the claims for specifics —
not much provided. Note that claim 25
is broad enough to encompass co-administration
of any two compounds that reduce serum
cholesterol.

Thanks

Dear Examiner,
You can help us in our efforts to get searches back to you in a timely manner by including your art unit and room number on all searches you submit to the STIC.
Thanks from the STIC-Biotech/Chemistry Library

STAFF USE ONLY

Date completed: 6/13/01
Searcher:
Terminal time:
Elapsed time:
CPU time: 30
Total time:
Number of Searches:
Number of Databases:

Search Site
- ___ STIC
- ✓ CM-1
- ___ Pre-S

Type of Search
- ___ N.A. Sequence
- ___ A.A. Sequence
- ___ Structure
- ✓ Bibliographic

Vendors
- ___ IG
- ✓ STN
- ___ Dialog
- ___ APS
- ___ Geninfo
- ___ SDC
- ___ DARC/Questel
- ___ Other

PTO-1590 (9-90)

=> fil reg
FILE 'REGISTRY' ENTERED AT 12:01:32 ON 23 JUN 2001
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

STRUCTURE FILE UPDATES: 22 JUN 2001 HIGHEST RN 343216-50-2
DICTIONARY FILE UPDATES: 22 JUN 2001 HIGHEST RN 343216-50-2

TSCA INFORMATION NOW CURRENT THROUGH January 11, 2001

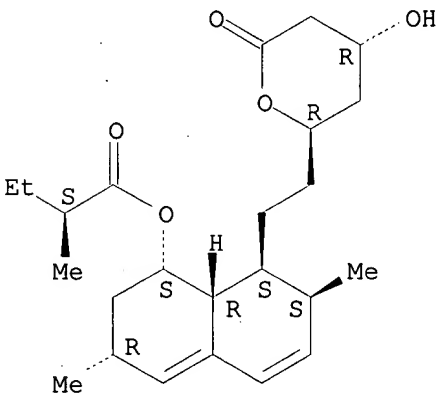
Please note that search-term pricing does apply when conducting SmartSELECT searches.

Structure search limits have been increased. See HELP SLIMIT for details.

=> d ide can tot

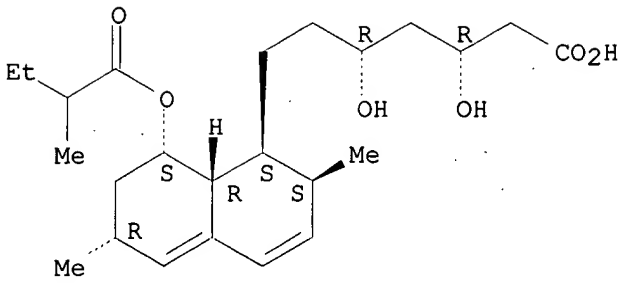
L85 ANSWER 1 OF 40 REGISTRY COPYRIGHT 2001 ACS
RN 316381-08-5 REGISTRY
CN **Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, labeled with tritium, (2S)- (9CI)** (CA INDEX NAME)
FS STEREOSEARCH
MF **C24 H36 O5**
SR CAS Registry Services
LC STN Files: CHEMCATS
IL XH-3

Absolute stereochemistry.



L85 ANSWER 2 OF 40 REGISTRY COPYRIGHT 2001 ACS
RN 314729-27-6 REGISTRY
CN **1-Naphthaleneheptanoic acid, 1,2,6,7,8,8a-hexahydro-.beta.,.delta.-dihydroxy-2,6-dimethyl-8-(2-methyl-1-oxobutoxy)-, (.beta.R,.delta.R,1S,2S,6R,8S,8aR)- (9CI)** (CA INDEX NAME)
FS STEREOSEARCH
MF **C24 H38 O6**
CI COM
SR CA
LC STN Files: CA, CAPLUS, CASREACT

Absolute stereochemistry.

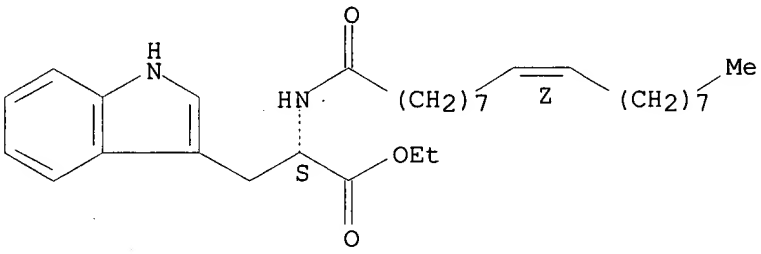


1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:71492

L85 ANSWER 3 OF 40 REGISTRY COPYRIGHT 2001 ACS
RN **261734-93-4** REGISTRY
CN L-Tryptophan, N-[(9Z)-1-oxo-9-octadecenyl]-, ethyl ester (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C31 H48 N2 O3
SR CA
LC STN Files: CA, CAPLUS, TOXLIT

Absolute stereochemistry.
Double bond geometry as shown.

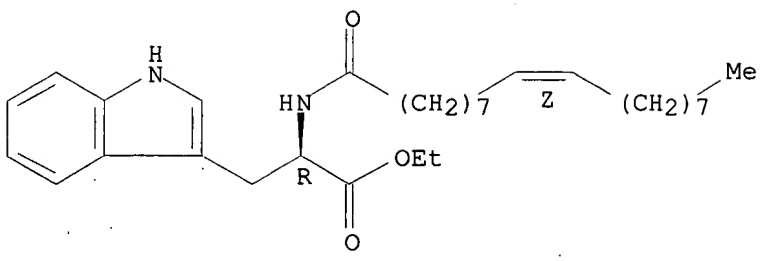


1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:231975

L85 ANSWER 4 OF 40 REGISTRY COPYRIGHT 2001 ACS
RN **261734-92-3** REGISTRY
CN D-Tryptophan, N-[(9Z)-1-oxo-9-octadecenyl]-, ethyl ester (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C31 H48 N2 O3
SR CA
LC STN Files: CA, CAPLUS, TOXLIT

Absolute stereochemistry.
Double bond geometry as shown.

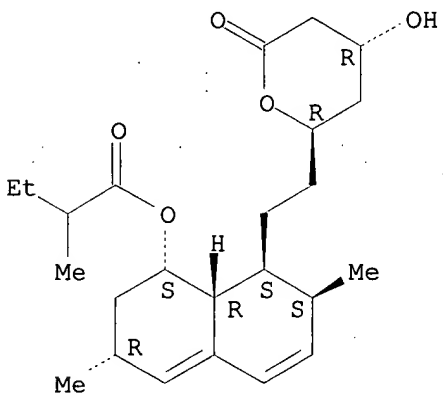


1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:231975

L85 ANSWER 5 OF 40 REGISTRY COPYRIGHT 2001 ACS
RN 237073-61-9 REGISTRY
CN **Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester (9CI)** (CA INDEX NAME)
FS STEREOSEARCH
MF **C24 H36 O5**
SR CA
LC STN Files: CA, CAPLUS, CASREACT, USPATFULL

Absolute stereochemistry.



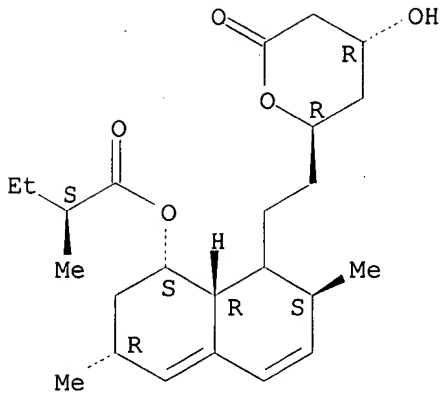
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:71492

REFERENCE 2: 131:157706

L85 ANSWER 6 OF 40 REGISTRY COPYRIGHT 2001 ACS
RN 214357-28-5 REGISTRY
CN **Butanoic acid, 2-methyl-, (1S,3R,7S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (9CI)** (CA INDEX NAME)
FS STEREOSEARCH
MF **C24 H36 O5**
SR CA
LC STN Files: CA, CAPLUS

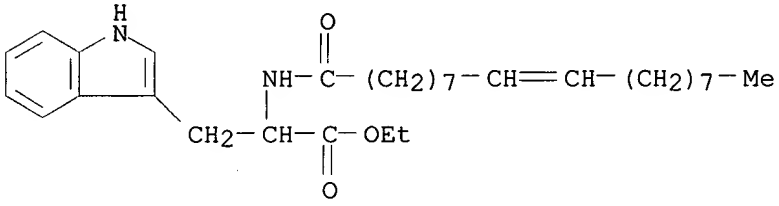
Absolute stereochemistry.



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 129:290016

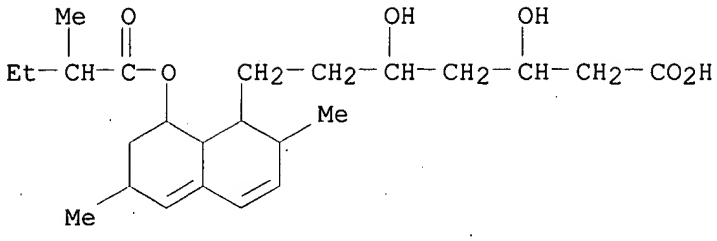
L85 ANSWER 7 OF 40 REGISTRY COPYRIGHT 2001 ACS
RN **202401-34-1** REGISTRY
CN Tryptophan, N-(1-oxo-9-octadecenyl)-, ethyl ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C31 H48 N2 O3
SR CAS Registry Services
LC STN Files: CA, CAPLUS, CHEMCATS, TOXLIT



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:371771

L85 ANSWER 8 OF 40 REGISTRY COPYRIGHT 2001 ACS
RN 137767-34-1 REGISTRY
CN **1-Naphthaleneheptanoic acid, 1,2,6,7,8,8a-hexahydro-.beta.,.delta.-dihydroxy-2,6-dimethyl-8-(2-methyl-1-oxobutoxy)- (9CI)** (CA INDEX NAME)
OTHER NAMES:
CN L 665465
MF **C24 H38 O6**
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS, TOXLIT
(*File contains numerically searchable property data)



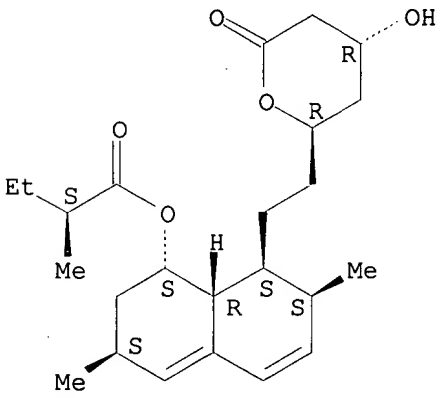
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 116:51291

REFERENCE 2: 116:537

L85 ANSWER 9 OF 40 REGISTRY COPYRIGHT 2001 ACS
RN 123049-73-0 REGISTRY
CN **Butanoic acid, 2-methyl-, 1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-(tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl)ethyl]-1-naphthalenyl ester, [1S-[1.alpha.(R*),3.beta.,7.beta.,8.beta.(2S*,4S*),8a.beta.]]- (9CI)** (CA INDEX NAME)
FS STEREOSEARCH
MF **C24 H36 O5**
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS, CHEMINFORMRX
(*File contains numerically searchable property data)

Absolute stereochemistry.



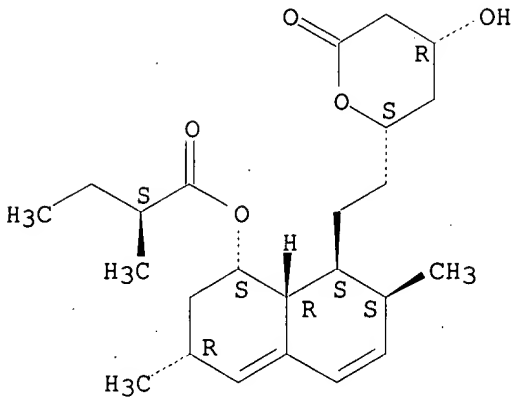
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 121:204880

REFERENCE 2: 111:173984

L85 ANSWER 10 OF 40 REGISTRY COPYRIGHT 2001 ACS
RN 105227-51-8 REGISTRY
CN **Butanoic acid, 2-methyl-, 1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-(tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl)ethyl]-1-naphthalenyl ester, [1S-[1.alpha.(R*),3.alpha.,7.beta.,8.beta.(2R*,4S*),8a.beta.]]- (9CI)** (CA INDEX NAME)
FS STEREOSEARCH
MF **C24 H36 O5**
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT, CHEMINFORMRX
(*File contains numerically searchable property data)

Absolute stereochemistry.



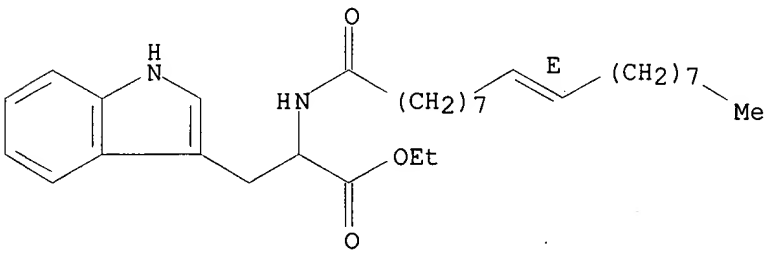
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 111:133822

REFERENCE 2: 106:49852

L85 ANSWER 11 OF 40 REGISTRY COPYRIGHT 2001 ACS
RN **94921-32-1** REGISTRY
CN Tryptophan, N-(1-oxo-9-octadecenyl)-, ethyl ester, (E)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN DL-Tryptophan, N-(1-oxo-9-octadecenyl)-, ethyl ester, (E)-
FS STEREOSEARCH
MF C31 H48 N2 O3
LC STN Files: BEILSTEIN*, CA, CAPLUS, TOXLIT
(*File contains numerically searchable property data)

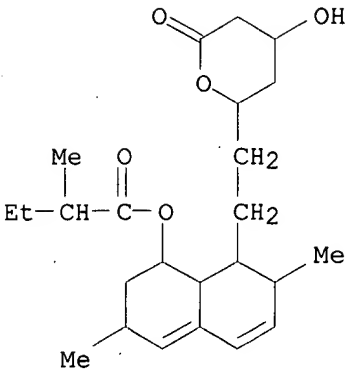
Double bond geometry as shown.



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 102:89686

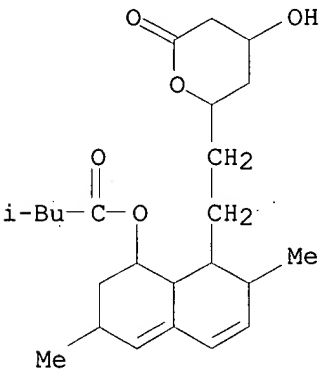
L85 ANSWER 12 OF 40 REGISTRY COPYRIGHT 2001 ACS
RN 83213-71-2 REGISTRY
CN **Butanoic acid, 2-methyl-, 1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-(tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl)ethyl]-1-naphthalenyl ester (9CI)** (CA INDEX NAME)
OTHER NAMES:
CN Monarubin
MF **C24 H36 O5**
LC STN Files: BEILSTEIN*, CA, CAPLUS, CHEMINFORMRX
(*File contains numerically searchable property data)



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 101:130443

L85 ANSWER 13 OF 40 REGISTRY COPYRIGHT 2001 ACS
RN 81202-26-8 REGISTRY
CN **Butanoic acid, 3-methyl-, 1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-(tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl)ethyl]-1-naphthalenyl ester (9CI)** (CA INDEX NAME)
MF **C24 H36 O5**
LC STN Files: BEILSTEIN*, CA, CAPLUS
(*File contains numerically searchable property data)



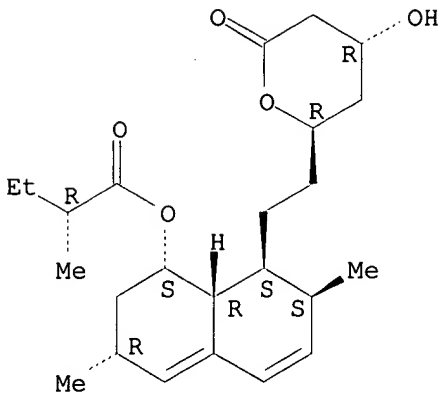
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 97:23627

REFERENCE 2: 96:181078

L85 ANSWER 14 OF 40 REGISTRY COPYRIGHT 2001 ACS
RN 79952-44-6 REGISTRY
CN **Butanoic acid, 2-methyl-, 1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-(tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl)ethyl]-1-naphthalenyl ester, [1S-[1.alpha.(S*),3.alpha.,7.beta.,8.beta.(2S*,4S*),8a.beta.]]- (9CI)** (CA INDEX NAME)
FS STEREOSEARCH
MF **C24 H36 O5**
LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT, CHEMINFORMRX, TOXLIT, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry.



9 REFERENCES IN FILE CA (1967 TO DATE)
9 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 111:133822

REFERENCE 2: 110:18101

REFERENCE 3: 104:186228

REFERENCE 4: 101:210982

REFERENCE 5: 101:130521

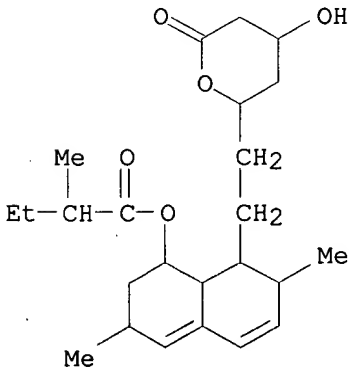
REFERENCE 6: 101:130443

REFERENCE 7: 97:127360

REFERENCE 8: 96:34985

REFERENCE 9: 95:219968

L85 ANSWER 15 OF 40 REGISTRY COPYRIGHT 2001 ACS
RN 79952-43-5 REGISTRY
CN **Butanoic acid, 2-methyl-, 1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-(tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl)ethyl]-1-naphthalenyl ester (9CI)** (CA INDEX NAME)
MF **C24 H36 O5**
LC STN Files: BEILSTEIN*, CA, CAPLUS, CHEMINFORMRX, USPATFULL
(*File contains numerically searchable property data)



10 REFERENCES IN FILE CA (1967 TO DATE)
10 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 128:140889

REFERENCE 2: 113:78161

REFERENCE 3: 112:7367

REFERENCE 4: 111:133822

REFERENCE 5: 101:210982

REFERENCE 6: 101:130521

REFERENCE 7: 101:130443

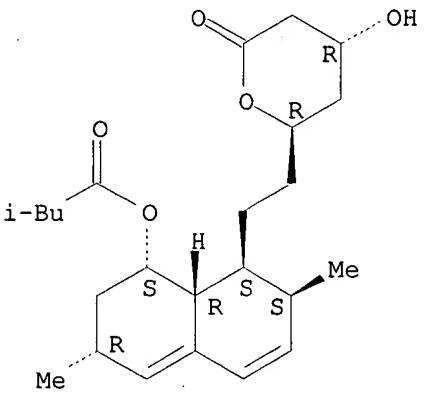
REFERENCE 8: 99:70288

REFERENCE 9: 96:34985

REFERENCE 10: 95:219968

L85 ANSWER 16 OF 40 REGISTRY COPYRIGHT 2001 ACS
RN 79902-41-3 REGISTRY
CN **Butanoic acid, 3-methyl-, 1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-(tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl)ethyl]-1-naphthalenyl ester, [1S-[1.alpha.,3.alpha.,7.beta.,8.beta.(2S*,4S*),8a.beta.]]- (9CI)** (CA INDEX NAME)
FS STEREOSEARCH
MF **C24 H36 O5**
LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT, TOXLIT, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry.



7 REFERENCES IN FILE CA (1967 TO DATE)
7 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 122:263678

REFERENCE 2: 110:18101

REFERENCE 3: 104:186228

REFERENCE 4: 101:210982

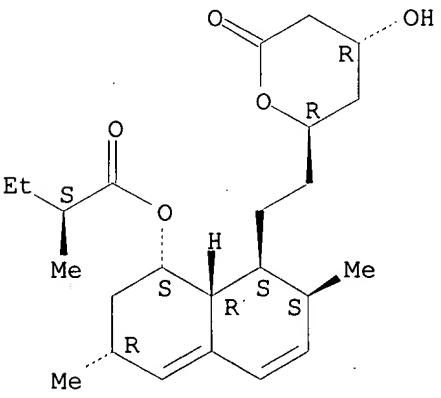
REFERENCE 5: 101:130521

REFERENCE 6: 96:34985

REFERENCE 7: 95:219968

L85 ANSWER 17 OF 40 REGISTRY COPYRIGHT 2001 ACS
RN **75330-75-5** REGISTRY
CN **Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **Butanoic acid, 2-methyl-, 1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-(tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl)ethyl]-1-naphthalenyl ester, [1S-[1.alpha.(R*),3.alpha.,7.beta.,8.beta.(2S*,4S*),8a.beta.]]-**
OTHER NAMES:
CN (+)-Mevinolin
CN Antibiotic MB 530B
CN L 154803
CN **Lovastatin**
CN Mevacor
CN Mevinolin
CN MK 803
CN Monacolin K
CN Monacolin K lactone
CN MSD 803
FS STEREOSEARCH
DR 71949-96-7, 74133-25-8, 81739-26-6
MF **C24 H36 O5**
CI COM
LC STN Files: AGRICOLA, AIDSLINE, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, HSDB*, IFICDB, IFIUDB, IMSDIRECTORY, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PHAR, PROMT, RTECS*, SPECINFO, SYNTHLINE, TOXLINE, TOXLIT, USAN, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO

Absolute stereochemistry.



1330 REFERENCES IN FILE CA (1967 TO DATE)
50 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1331 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:10035

REFERENCE 2: 135:2587

REFERENCE 3: 135:364

REFERENCE 4: 135:363

REFERENCE 5: 134:371882

REFERENCE 6: 134:365738

REFERENCE 7: 134:362292

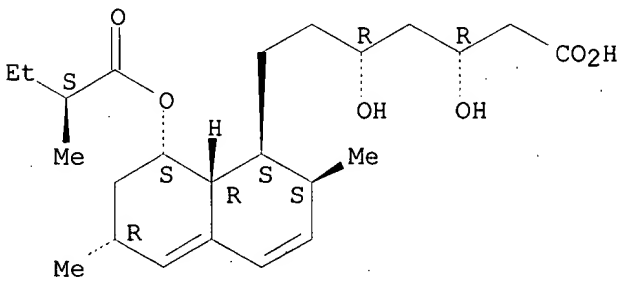
REFERENCE 8: 134:361140

REFERENCE 9: 134:361049

REFERENCE 10: 134:357587

L85 ANSWER 18 OF 40 REGISTRY COPYRIGHT 2001 ACS
RN 75225-51-3 REGISTRY
CN **1-Naphthaleneheptanoic acid, 1,2,6,7,8,8a-hexahydro-.beta.,.delta.-dihydroxy-2,6-dimethyl-8-[(2S)-2-methyl-1-oxobutoxy]-, (.beta.R,.delta.R,1S,2S,6R,8S,8aR)- (9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **1-Naphthaleneheptanoic acid, 1,2,6,7,8,8a-hexahydro-.beta.,.delta.-dihydroxy-2,6-dimethyl-8-(2-methyl-1-oxobutoxy)-, [1S-[1.alpha.(.beta.S*,.delta.S*),2.alpha.,6.beta.,8.beta.(R*),8a.alpha.]]-**
OTHER NAMES:
CN L 154819
CN **Lovastatin acid**
CN Mevinolinic acid
CN MK 819
CN Monacolinic K acid
CN MSD 803 acid
CN MSD 803 free acid
FS STEREOSEARCH
DR 76556-02-0, 77285-87-1
MF **C24 H38 O6**
CI COM
LC STN Files: AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, DDFU, DRUGU, EMBASE, IPA, MEDLINE, NAPRALERT, RTECS*, TOXLINE, TOXLIT, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry.



72 REFERENCES IN FILE CA (1967 TO DATE)
7 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
72 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:336227

REFERENCE 2: 134:325321

REFERENCE 3: 134:304920

REFERENCE 4: 134:275767

REFERENCE 5: 134:188026

REFERENCE 6: 133:3757

REFERENCE 7: 132:278495

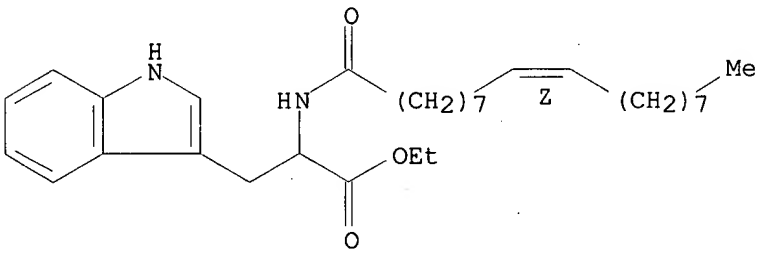
REFERENCE 8: 132:278494

REFERENCE 9: 132:241979

REFERENCE 10: 132:202648

L85 ANSWER 19 OF 40 REGISTRY COPYRIGHT 2001 ACS
RN **71806-22-9** REGISTRY
CN Tryptophan, N-[(9Z)-1-oxo-9-octadecenyl]-, ethyl ester (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN DL-Tryptophan, N-(1-oxo-9-octadecenyl)-, ethyl ester, (Z)-
OTHER NAMES:
CN Tryptophan, N-(1-oxo-9-octadecenyl)-, ethyl ester, (Z)-
FS STEREOSEARCH
MF C31 H48 N2 O3
LC STN Files: BEILSTEIN*, CA, CAPLUS, CHEMCATS, MEDLINE, TOXLIT, USPATFULL
(*File contains numerically searchable property data)

Double bond geometry as shown.



6 REFERENCES IN FILE CA (1967 TO DATE)
6 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 129:402

REFERENCE 2: 102:89686

REFERENCE 3: 101:152341

REFERENCE 4: 100:45116

REFERENCE 5: 94:174880

REFERENCE 6: 91:193639

L85 ANSWER 20 OF 40 REGISTRY COPYRIGHT 2001 ACS
RN **65589-58-4** REGISTRY
CN Agar, hydrogen sulfate (9CI) (CA INDEX NAME)
MF H2 O4 S . x Unspecified
PCT Manual registration
LC STN Files: CA, CAPLUS, CHEMLIST, TOXLIT, USPATFULL
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)

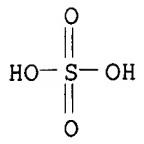
CM 1

CRN 9002-18-0
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 2

CRN 7664-93-9
CMF H2 O4 S



6 REFERENCES IN FILE CA (1967 TO DATE)
6 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 126:297659

REFERENCE 2: 103:179896

REFERENCE 3: 103:179895

REFERENCE 4: 92:15572

REFERENCE 5: 88:146096

REFERENCE 6: 88:83512

L85 ANSWER 21 OF 40 REGISTRY COPYRIGHT 2001 ACS
RN **37293-26-8** REGISTRY
CN Chitosan, hydrogen sulfate (ester) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Chitosan polysulfate
CN Chitosan sulfate
MF H2 O4 S . x Unspecified
CI COM
PCT Manual registration
LC STN Files: BIOSIS, CA, CAPLUS, DDFU, DRUGU, IFICDB, IFIPAT, IFIUDB, PIRA, PROMT, TOXLIT, USPATFULL

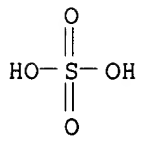
CM 1

CRN 9012-76-4
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 2

CRN 7664-93-9
CMF H2 O4 S



71 REFERENCES IN FILE CA (1967 TO DATE)
8 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
71 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:168390

REFERENCE 2: 133:297783

REFERENCE 3: 133:168289

REFERENCE 4: 133:147274

REFERENCE 5: 132:284193

REFERENCE 6: 132:207622

REFERENCE 7: 131:314156

REFERENCE 8: 131:311873

REFERENCE 9: 131:233584

REFERENCE 10: 131:63497

L85 ANSWER 22 OF 40 REGISTRY COPYRIGHT 2001 ACS
RN **9049-31-4** REGISTRY
CN Alginic acid, hydrogen sulfate (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Algin sulfate
CN Alginic acid sulfate
MF H2 O4 S . x Unspecified
CI COM
PCT Manual registration
LC STN Files: BIOSIS, CA, CAPLUS, NAPRALERT, TOXLIT, USPATFULL

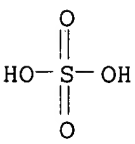
CM 1

CRN 9005-32-7
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 2

CRN 7664-93-9
CMF H2 O4 S



22 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
22 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:155175

REFERENCE 2: 133:147274

REFERENCE 3: 129:2249

REFERENCE 4: 128:317217

REFERENCE 5: 126:297659

REFERENCE 6: 125:76389

REFERENCE 7: 122:222702

REFERENCE 8: 121:91354

REFERENCE 9: 120:95787

REFERENCE 10: 117:257993

L85 ANSWER 23 OF 40 REGISTRY COPYRIGHT 2001 ACS
RN **9047-13-6** REGISTRY
CN Amylopectin, hydrogen sulfate (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Amylopectin sulfate
CN Sulfated amylopectin
MF H2 O4 S . x Unspecified
PCT Manual registration
LC STN Files: BIOSIS, CA, CANCERLIT, CAPLUS, EMBASE, MEDLINE, RTECS*, TOXLINE, TOXLIT, USPATFULL
(*File contains numerically searchable property data)

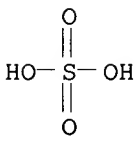
CM 1

CRN 9037-22-3
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 2

CRN 7664-93-9
CMF H2 O4 S



33 REFERENCES IN FILE CA (1967 TO DATE)
3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
33 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 126:297659

REFERENCE 2: 125:109645

REFERENCE 3: 121:6622

REFERENCE 4: 119:133233

REFERENCE 5: 116:99057

REFERENCE 6: 111:739

REFERENCE 7: 106:190869

REFERENCE 8: 103:64471

REFERENCE 9: 102:110545

REFERENCE 10: 99:124377

L85 ANSWER 24 OF 40 REGISTRY COPYRIGHT 2001 ACS
RN **9042-14-2** REGISTRY
CN Dextran, hydrogen sulfate (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Dextran polysulfate
CN Dextran sulfate
CN Dextran sulfate 500
CN Dextran sulfate 5000
CN Dextran sulfuric acid
CN Dextran sulphate
CN MDS-Kowa
CN NSC 620255
CN PF 51
CN PF 51 (carbohydrate)
CN Polydextran sulfate
CN Polyglucin, sulfate
CN Sulfopolyglucin
CN T 500
DR 9057-27-6, 9063-02-9, 50935-34-7, 37271-05-9, 73075-68-0, 191288-77-4
MF H2 O4 S . x Unspecified
CI COM
PCT Manual registration, Polyother, Polyother only
LC STN Files: ADISINSIGHT, AGRICOLA, AIDSLINE, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, NIOSHTIC, PIRA, PROMT, RTECS*, TOXLINE, TOXLIT, USAN, USPATFULL, VTB
(*File contains numerically searchable property data)
Other Sources: NDSL**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

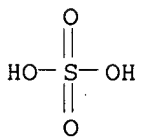
CM 1

CRN 9004-54-0
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 2

CRN 7664-93-9
CMF H2 O4 S



2331 REFERENCES IN FILE CA (1967 TO DATE)
155 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2331 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:10087

REFERENCE 2: 135:4580

REFERENCE 3: 135:2524

REFERENCE 4: 135:485

REFERENCE 5: 134:361390

REFERENCE 6: 134:331616

REFERENCE 7: 134:325204

REFERENCE 8: 134:322477

REFERENCE 9: 134:320868

REFERENCE 10: 134:316194

L85 ANSWER 25 OF 40 REGISTRY COPYRIGHT 2001 ACS
RN **9037-22-3** REGISTRY
CN Amylopectin (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Amaizo 839
CN Amioca
CN Amioca WCS
CN C*Pharm 12018
CN Cato 225
CN Cato 240
CN Cato 270
CN Farinex WM 85
CN Film Kote 54
CN Honen Alpha Waxy Starch
CN Kosol
CN Pectin, amylo
CN Starch, waxy
CN Ultraamylopectin N
CN Ultrasperse A
CN Waxy 7350
CN Waxy corn starch
CN Waxy maize starch
CN Waxy starch
CN WCS
DR 9050-86-6, 189047-96-9
MF Unspecified
CI PMS, COM, MAN
PCT Manual registration, Polyother, Polyother only
LC STN Files: AGRICOLA, AIDSLINE, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, NAPRALERT, PIRA, PROMT, TOXLINE, TOXLIT, TULSA, USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
2428 REFERENCES IN FILE CA (1967 TO DATE)
182 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2431 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:3149

REFERENCE 2: 134:365927

REFERENCE 3: 134:365921

REFERENCE 4: 134:354771

REFERENCE 5: 134:354765

REFERENCE 6: 134:352542

REFERENCE 7: 134:352532

REFERENCE 8: 134:339847

REFERENCE 9: 134:339804

REFERENCE 10: 134:337490

L85 ANSWER 26 OF 40 REGISTRY COPYRIGHT 2001 ACS
RN **9032-43-3** REGISTRY
CN Cellulose, hydrogen sulfate (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Cellulose sulfate
CN Sulfate cellulose
CN Sulfocellulose
DR 166736-01-2, 55187-33-2
MF H2 O4 S . x Unspecified
CI COM
PCT Manual registration
LC STN Files: AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CBNB, CIN, DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, MEDLINE, PIRA, PROMT, TOXLINE, TOXLIT, TULSA, USPATFULL

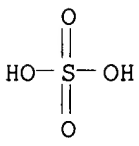
CM 1

CRN 9004-34-6
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 2

CRN 7664-93-9
CMF H2 O4 S



401 REFERENCES IN FILE CA (1967 TO DATE)
46 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
401 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:4580

REFERENCE 2: 134:174523

REFERENCE 3: 134:163843

REFERENCE 4: 134:117314

REFERENCE 5: 134:73167

REFERENCE 6: 134:44011

REFERENCE 7: 133:340251

REFERENCE 8: 133:305579

REFERENCE 9: 133:283174

REFERENCE 10: 133:271421

L85 ANSWER 27 OF 40 REGISTRY COPYRIGHT 2001 ACS

RN **9027-63-8** REGISTRY
CN Acyltransferase, cholesterol (9CI) (CA INDEX NAME)
OTHER NAMES:
CN ACAT
CN Acyl coenzyme A-cholesterol O-acyltransferase
CN Acyl-CoA:cholesteryl acyltransferase
CN Acyl-coenzyme A-sterol acyltransferase
CN Acyl-coenzyme A:cholesterol acyltransferase
CN AcylCoA-Cholesterol acytransferase
CN AcylCoA-cholesterol O-acyltransferase
CN Cholesterol acyltransferase
CN Cholesterol ester synthase
CN Cholesterol ester synthetase
CN Cholesteryl ester synthetase
CN E.C. 2.3.1.26
CN Steryl ester synthase
MF Unspecified
CI MAN
LC STN Files: AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CAPLUS, CBNB, CEN, CIN, EMBASE, PROMT, TOXLIT, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
1482 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1482 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:3664

REFERENCE 2: 135:1241

REFERENCE 3: 135:369

REFERENCE 4: 134:371771

REFERENCE 5: 134:338258

REFERENCE 6: 134:337498

REFERENCE 7: 134:323882

REFERENCE 8: 134:323687

REFERENCE 9: 134:321178

REFERENCE 10: 134:311218

L85 ANSWER 28 OF 40 REGISTRY COPYRIGHT 2001 ACS
RN **9026-00-0** REGISTRY
CN Esterase, cholesterol (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Cholesterase
CN Cholesterin esterase
CN Cholesterol ester hydrolase
CN Cholesterol esterase
CN Cholesteryl ester hydrolase
CN Cholesteryl esterase
CN E.C. 3.1.1.13
CN Lysosomal acid lipase
CN Neutral cholesteryl ester hydrolase
CN Sterol ester hydrolase
CN Sterol esterase
DR 9040-56-6
MF Unspecified
CI MAN
LC STN Files: AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CAPLUS, CASREACT, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, EMBASE,

IFICDB, IFIPAT, IFIUDB, PROMT, TOXLIT, USPATFULL
Other Sources: EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
1552 REFERENCES IN FILE CA (1967 TO DATE)
21 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1552 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:1241

REFERENCE 2: 134:362292

REFERENCE 3: 134:353586

REFERENCE 4: 134:350257

REFERENCE 5: 134:348257

REFERENCE 6: 134:323855

REFERENCE 7: 134:320830

REFERENCE 8: 134:292266

REFERENCE 9: 134:249944

REFERENCE 10: 134:249194

L85 ANSWER 29 OF 40 REGISTRY COPYRIGHT 2001 ACS
RN **9012-77-5** REGISTRY
CN Pectin, hydrogen sulfate (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Pectin polysulfate
DR 37221-19-5
MF H2 O4 S . x Unspecified
CI COM
PCT Manual registration
LC STN Files: CA, CAPLUS, IFICDB, IFIPAT, IFIUDB, TOXLIT, USPATFULL

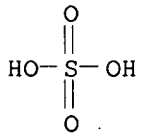
CM 1

CRN 9000-69-5
CMF Unspecified
CCI PMS, MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

CM 2

CRN 7664-93-9
CMF H2 O4 S



7 REFERENCES IN FILE CA (1967 TO DATE)
7 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:147274

REFERENCE 2: 126:297659

REFERENCE 3: 83:12708

REFERENCE 4: 82:103170

REFERENCE 5: 79:20613

REFERENCE 6: 78:126096

REFERENCE 7: 77:77034

L85 ANSWER 30 OF 40 REGISTRY COPYRIGHT 2001 ACS
RN **9012-76-4** REGISTRY
CN Chitosan (8CI, 9CI) (CA INDEX NAME)
OTHER NAMES:
CN 100D-VL
CN Biopolymer L 112
CN Chicol
CN Chitan, N-acetyl-
CN Chitin, N-deacetyl-
CN Chitofine
CN Chitopearl 3510
CN Chitopearl BC 3000
CN Chitopearl BCW 2500
CN Chitopearl BCW 3000
CN Chitopearl BCW 3500
CN Chitopearl BCW 3505
CN Chitopearl BCW 3507
CN Chitosan 500
CN Chitosan CLH
CN Chitosan EL
CN Chitosan F
CN Chitosan FL
CN Chitosan H
CN Chitosan LL
CN Chitosan LL 80
CN Chitosan LLWP
CN Chitosan M
CN Chitosan MP
CN Chitosan SK 10
CN Chitosan VL
CN Chitosom
CN Crystan LA-S
CN CTA 1 Lactic Acid
CN CTA 4
CN DAC 50
CN DAC 70
CN Daichitosan VL
CN Daichitosan W 10
CN Deacetylchitin
CN FCM 117
CN Flonac C
CN Flonac N
CN HC 1
CN HC 1 (polysaccharide)
CN Hiset KW 5
CN Hydagen CMFP
CN Hydagen HCMF
CN Kimitsu Chitosan F
CN Kimitsu Chitosan F 2
CN Kimitsu Chitosan F 2P
CN Kimitsu Chitosan H
CN Kimitsu Chitosan L
CN Kimitsu Chitosan LL
CN Kimitsu Chitosan LLW

ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for DISPLAY
DR 57285-05-9
MF Unspecified
CI PMS, COM, MAN
PCT Manual registration, Polyother, Polyother only
LC STN Files: AGRICOLA, AIDSLINE, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DIOGENES, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, NAPRALERT, PHAR, PIRA, PROMT, RTECS*, TOXLINE, TOXLIT, TULSA, USAN, USPATFULL, VTB
(*File contains numerically searchable property data)
Other Sources: NDSL**, TSCA**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
8810 REFERENCES IN FILE CA (1967 TO DATE)
1695 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
8835 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:10087

REFERENCE 2: 135:10066

REFERENCE 3: 135:10022

REFERENCE 4: 135:9998

REFERENCE 5: 135:9941

REFERENCE 6: 135:9907

REFERENCE 7: 135:9880

REFERENCE 8: 135:9398

REFERENCE 9: 135:9395

REFERENCE 10: 135:9376

L85 ANSWER 31 OF 40 REGISTRY COPYRIGHT 2001 ACS
RN **9005-49-6** REGISTRY
CN Heparin (8CI, 9CI) (CA INDEX NAME)
OTHER NAMES:
CN .alpha.-Heparin
CN Bemiparin
CN Certoparin
CN Clexane
CN Clivarin
CN Clivarine
CN CY 216
CN CY 222
CN Dalteparin
CN Enoxaparin
CN Fluxum
CN FR 860
CN Fragmin A
CN Fragmin B
CN Fraxiparin
CN Heparin sulfate
CN Heparinic acid
CN KB 101
CN Multiparin
CN Novoheparin
CN OP 386
CN OP 622

CN Pabyrn
CN Parnaparin
CN Parvoparin
CN Reviparin
CN Sandoparin
CN Sublingula
CN Vetren
CN Vitrum AB
DR 9075-96-1, 11078-24-3, 11129-39-8, 104521-37-1, 37324-73-5, 91449-79-5
MF Unspecified
CI PMS, COM, MAN
PCT Manual registration, Polyester, Polyester formed
LC STN Files: AGRICOLA, AIDSLINE, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IMSDIRECTORY, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PHAR, PIRA, PROMT, RTECS*, TOXLINE, TOXLIT, USAN, USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
17089 REFERENCES IN FILE CA (1967 TO DATE)
1710 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
17101 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:10062

REFERENCE 2: 135:10016

REFERENCE 3: 135:2500

REFERENCE 4: 135:1998

REFERENCE 5: 135:1890

REFERENCE 6: 135:485

REFERENCE 7: 135:342

REFERENCE 8: 135:303

REFERENCE 9: 135:298

REFERENCE 10: 135:291

L85 ANSWER 32 OF 40 REGISTRY COPYRIGHT 2001 ACS
RN **9005-38-3** REGISTRY
CN Alginic acid, sodium salt (8CI, 9CI) (CA INDEX NAME)
OTHER NAMES:
CN 1-3F
CN A 7C618
CN Algin
CN Algin (polysaccharide)
CN Algin ML
CN Alginate FD 155
CN Alginate KMF
CN Alginate TBVV/N 2
CN Algipon L 1168
CN Algitex LL
CN Algitex M
CN Algogel HV
CN Algogel LV
CN Algogel MV
CN Algogel MVR

CN Alloid G
CN Amnucol
CN Antimigrant C 45
CN Cecalginate HV 600
CN Cecalginate HV/KL 600
CN Cecalgine TBV
CN CHT Alginate EHV
CN CHT Alginate MV
CN Cohasal IH
CN Darid QH
CN Dariloid QH
CN Dialgin HV
CN Duck Algin
CN Duck Algin EX 30
CN Duck Algin NSPH
CN Duck Algin NSPL
CN Duck Algin NSPLL
CN Duck Algin NSPM
CN Duck Algin S
CN EHV
CN Halltex
CN IL 2
CN Kelco Gel HV
CN Kelco Gel LV
CN Kelcosol
CN Kelgin
CN Kelgin F
CN Kelgin HV
CN Kelgin LV
CN Kelgin MV
CN Kelgin QH
CN Kelgin QM
CN Kelgin RL
CN Kelgin XL
CN Kelp Algin L
ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for DISPLAY
DR 12772-46-2, 9005-40-7, 56940-21-7, 56940-22-8, 63278-91-1, 50643-02-2, 77030-65-0, 81989-21-1, 32129-82-1, 32197-42-5
MF Unspecified
CI PMS, COM, MAN
PCT Manual registration, Polyester, Polyester formed
LC STN Files: AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, DETHERM*, DIOGENES, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IMSDIRECTORY, IPA, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PIRA, PROMT, RTECS*, TOXLINE, TOXLIT, TULSA, USAN, USPATFULL, VTB
(*File contains numerically searchable property data)
Other Sources: DSL**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
6571 REFERENCES IN FILE CA (1967 TO DATE)
154 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
6575 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:10016

REFERENCE 2: 135:9786

REFERENCE 3: 135:4871

REFERENCE 4: 135:4734

REFERENCE 5: 135:2848

REFERENCE 6: 134:373026

REFERENCE 7: 134:371799

REFERENCE 8: 134:371776

REFERENCE 9: 134:371718

REFERENCE 10: 134:368947

L85 ANSWER 33 OF 40 REGISTRY COPYRIGHT 2001 ACS
RN **9005-32-7** REGISTRY
CN Alginic acid (8CI, 9CI) (CA INDEX NAME)
OTHER NAMES:
CN A 2830-9
CN Acid Algin G 2
CN Kelacid
CN Landalgine
CN Norgine
CN Protanal LF
CN Satialgine-H 8
CN Snow acid algin G
CN Verdyol Super
DR 210888-24-7
MF Unspecified
CI PMS, COM, MAN
PCT Manual registration, Polyester, Polyester formed
LC STN Files: AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CHEMSAFE, CIN, CSCHEM, DDFU, DIOGENES, DRUGU, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PIRA, PROMT, RTECS*, TOXLINE, TOXLIT, USAN, USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
5047 REFERENCES IN FILE CA (1967 TO DATE)
1188 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
5052 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:10038

REFERENCE 2: 135:9786

REFERENCE 3: 135:7315

REFERENCE 4: 135:7198

REFERENCE 5: 135:7186

REFERENCE 6: 135:4828

REFERENCE 7: 135:4565

REFERENCE 8: 135:2523

REFERENCE 9: 135:1638

REFERENCE 10: 134:371859

L85 ANSWER 34 OF 40 REGISTRY COPYRIGHT 2001 ACS
RN **9004-54-0** REGISTRY
CN Dextran (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Dextrans (8CI)

OTHER NAMES:
CN .alpha.-Dextran
CN CDC-H
CN DEX 500
CN Dextran 1.5
CN Dextran 10
CN Dextran 1000
CN Dextran 110
CN Dextran 15
CN Dextran 150
CN Dextran 2000
CN Dextran 250
CN Dextran 3000
CN Dextran 40
CN Dextran 45
CN Dextran 500
CN Dextran 60
CN Dextran 70
CN Dextran 75
CN Dextran B 512
CN Dextran B1355
CN Dextran D 10
CN Dextran PL 1S
CN Dextran PT 25
CN Dextran PVD
CN Dextran RMI
CN Dextran T 10
CN Dextran T 110
CN Dextran T 150
CN Dextran T 20
CN Dextran T 2000
CN Dextran T 500
CN Dextran T 70
CN Dextranen
CN Dextraven
CN Eudextran
CN Expandex
CN Gentran
CN Hemodex
CN Hyscon
CN Hyskon
CN Infucoll
CN Intrader
CN Intradex
CN LMD
CN LMWD
CN LU 122
CN LVD
CN Macrodex
CN Macrose
ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for DISPLAY
DR 12626-85-6, 9013-80-3, 9044-66-0, 11104-36-2, 11121-03-2, 37224-17-2, 86280-85-5
MF Unspecified
CI PMS, COM, MAN
PCT Manual registration, Polyother, Polyother only
LC STN Files: AGRICOLA, AIDSLINE, ANABSTR, BIOBUSINESS, BIOSIS, CA, CABA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DETHERM*, DIOGENES, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IMSDIRECTORY, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PHAR, PIRA, PROMT, RTECS*, TOXLINE, TOXLIT, TULSA, USAN, USPATFULL, VTB
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
10071 REFERENCES IN FILE CA (1967 TO DATE)
1994 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
10084 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:10005

REFERENCE 2: 135:9952

REFERENCE 3: 135:6233

REFERENCE 4: 135:4537

REFERENCE 5: 135:4302

REFERENCE 6: 135:2558

REFERENCE 7: 135:2539

REFERENCE 8: 135:2370

REFERENCE 9: 135:2366

REFERENCE 10: 134:371815

L85 ANSWER 35 OF 40 REGISTRY COPYRIGHT 2001 ACS
RN **9004-34-6** REGISTRY
CN Cellulose (8CI, 9CI) (CA INDEX NAME)
OTHER NAMES:
CN .alpha.-Cellulose
CN .beta.-Amylose
CN 3mAQUACEL
CN 402-2B
CN Alicell LV
CN Alpha Cel PB 25
CN Alphafloc
CN Arbocel
CN Arbocel B 00
CN Arbocel B 600/30
CN Arbocel B 800
CN Arbocel B 820C
CN Arbocel BC 1000
CN Arbocel BC 200
CN Arbocel BE 600
CN Arbocel BE 600/10
CN Arbocel BE 600/20
CN Arbocel BE 600/30
CN Arbocel BWW 40
CN Arbocel DC 1000
CN Arbocel FD 00
CN Arbocel FD 600/30
CN Arbocel FIC 200
CN Arbocel FT 40
CN Arbocel FT 600/30H
CN Arbocel TF 30HG
CN Arbocel TP 40
CN Avicel
CN Avicel 101
CN Avicel 102
CN Avicel 2330
CN Avicel 2331
CN Avicel 955
CN Avicel CL 611
CN Avicel E 200
CN Avicel F 20
CN Avicel FD 100

CN Avicel FD 101
CN Avicel FD-F 20
CN Avicel M 06
CN Avicel M 15
CN Avicel M 25
CN Avicel PH 101
CN Avicel PH 102
CN Avicel PH 105
CN Avicel PH 200
CN Avicel PH 301
CN Avicel PH 302
CN Avicel PH-F 10
CN Avicel PH-F 20
ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for DISPLAY
DR 12656-52-9, 9012-19-5, 9037-50-7, 9076-30-6, 58968-67-5, 99331-82-5, 67016-75-5, 67016-76-6, 51395-76-7, 61991-21-7, 61991-22-8, 68073-05-2, 70225-79-5, 74623-16-8, 75398-83-3, 77907-70-1, 84503-75-3, 89468-66-6, 39394-43-9
MF Unspecified
CI PMS, COM, MAN
PCT Manual registration, Polyother, Polyother only
LC STN Files: AGRICOLA, AIDSLINE, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CHEMSAFE, CIN, CSCHEM, CSNB, DDFU, DIOGENES, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PIRA, PROMT, RTECS*, TOXLINE, TOXLIT, TULSA, ULIDAT, USAN, USPATFULL, VTB
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
52993 REFERENCES IN FILE CA (1967 TO DATE)
6305 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
53044 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:13072

REFERENCE 2: 135:10102

REFERENCE 3: 135:10072

REFERENCE 4: 135:10071

REFERENCE 5: 135:10070

REFERENCE 6: 135:10069

REFERENCE 7: 135:10023

REFERENCE 8: 135:10021

REFERENCE 9: 135:10020

REFERENCE 10: 135:9877

L85 ANSWER 36 OF 40 REGISTRY COPYRIGHT 2001 ACS
RN **9002-18-0** REGISTRY
CN Agar (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Agar-agar (8CI)
OTHER NAMES:
CN Agar Agar Flake
CN Agargel
CN Agaropectin, mixt. with agarose

CN Agarose, mixt. with agaropectin
CN Bacto-agar
CN Bengal gelatin
CN Bengal isinglass
CN Ceylon isinglass
CN Chinese isinglass
CN D 100
CN D 100 (polysaccharide)
CN Deltagar LTS
CN Difco Bacto agar
CN Digenea simplex mucilage
CN GAM medium
CN Gelose
CN Japan agar
CN Japan isinglass
CN Kantenmatsu
CN Layor Carang
CN Luxara 1253
CN Oxoid III
CN Oxoid L 11
CN Phytagar
CN S 100
CN S 100 (polysaccharide)
CN UP 37
MF Unspecified
CI PMS, COM, MAN
PCT Manual registration, Polyother, Polyother only
LC STN Files: AGRICOLA, AIDSLINE, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAPLUS, CASREACT, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DIOGENES, DRUGU, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PIRA, PROMT, RTECS*, SPECINFO, TOXLINE, TOXLIT, TULSA, USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
3655 REFERENCES IN FILE CA (1967 TO DATE)
76 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
3658 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:4873

REFERENCE 2: 135:4734

REFERENCE 3: 135:3035

REFERENCE 4: 135:2556

REFERENCE 5: 134:371808

REFERENCE 6: 134:371776

REFERENCE 7: 134:366055

REFERENCE 8: 134:365957

REFERENCE 9: 134:365838

REFERENCE 10: 134:364102

L85 ANSWER 37 OF 40 REGISTRY COPYRIGHT 2001 ACS
RN **9000-69-5** REGISTRY
CN Pectin (9CI) (CA INDEX NAME)
OTHER NAMES:
CN AF 701

CN Cesapectin
CN Colyer pectin
CN D-D Slowset
CN Genu JMJ 100
CN Genu Pectin L 200
CN Genu Pectin LM 101AS
CN Genu Pectin LM 104AS
CN Genu Pectin LM 104AS-FS
CN Genu Pectin LM 18CG-Z
CN Genu Pectin X 0905
CN Genu Pectin YM 100
CN H&F Pectin Classic AF 701
CN LM 12CG-Z
CN LMNA/P 3450NA95
CN Marpee NL
CN Marpee OM
CN Methoxypectin
CN Methyl pectin
CN Methyl pectinate
CN MexPec 1400
CN Mexpectin XSS 100
CN Pectin 1694
CN Pectinate
CN Pectinic acid
CN Pectins
CN Slendid 200
CN Splendid
CN Unipectin
CN Unipectine 3450NA95
CN Unipectine RS 150.degree. SAG
CN USP 100
DR 9046-41-7, 9047-18-1
MF Unspecified
CI PMS, COM, MAN
PCT Manual registration, Polyother, Polyother only
LC STN Files: AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DIOGENES, DRUGU, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PDLCOM*, PIRA, PROMT, RTECS*, TOXLINE, TOXLIT, TULSA, USAN, USPATFULL, VTB
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
7478 REFERENCES IN FILE CA (1967 TO DATE)
388 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
7479 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:10020

REFERENCE 2: 135:7092

REFERENCE 3: 135:4949

REFERENCE 4: 135:4866

REFERENCE 5: 135:4863

REFERENCE 6: 135:4794

REFERENCE 7: 135:4710

REFERENCE 8: 135:4700

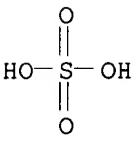
REFERENCE 9: 135:4565

REFERENCE 10: 135:4506

L85 ANSWER 38 OF 40 REGISTRY COPYRIGHT 2001 ACS
RN **1398-62-5** REGISTRY
CN Chitin, hydrogen sulfate (ester) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Chitin, sulfate (8CI)
MF H2 O4 S . x Unspecified
CI COM
PCT Manual registration
LC STN Files: BIOSIS, CA, CAPLUS, TOXLIT, USPATFULL

CM 1

CRN 7664-93-9
CMF H2 O4 S



CM 2

CRN 1398-61-4
CMF Unspecified
CCI MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
47 REFERENCES IN FILE CA (1967 TO DATE)
3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
47 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:147274

REFERENCE 2: 129:280954

REFERENCE 3: 129:92501

REFERENCE 4: 128:256454

REFERENCE 5: 128:158820

REFERENCE 6: 127:126352

REFERENCE 7: 126:297659

REFERENCE 8: 125:293042

REFERENCE 9: 125:269867

REFERENCE 10: 124:279167

L85 ANSWER 39 OF 40 REGISTRY COPYRIGHT 2001 ACS
RN **1398-61-4** REGISTRY
CN Chitin (8CI, 9CI) (CA INDEX NAME)
OTHER NAMES:
CN Chitan, N-acetyl-
CN Chitin Tc-L
CN Clandosan
CN Kimitsu Chitin

CN Regitex FA
DR 9043-70-3, 191802-95-6
MF Unspecified
CI COM, MAN
LC STN Files: AGRICOLA, AIDSLINE, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, NAPRALERT, PROMT, RTECS*, TOXLINE, TOXLIT, USPATFULL, VETU, VTB
(*File contains numerically searchable property data)
Other Sources: EINECS**, NDSL**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
5496 REFERENCES IN FILE CA (1967 TO DATE)
739 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
5504 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:9941

REFERENCE 2: 135:9810

REFERENCE 3: 135:7204

REFERENCE 4: 135:4535

REFERENCE 5: 135:3074

REFERENCE 6: 135:2868

REFERENCE 7: 135:2624

REFERENCE 8: 135:2192

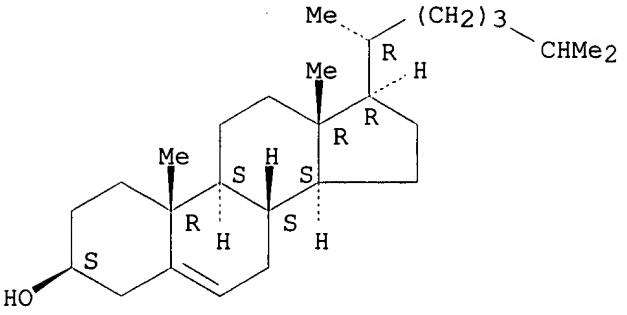
REFERENCE 9: 134:366147

REFERENCE 10: 134:365861

L85 ANSWER 40 OF 40 REGISTRY COPYRIGHT 2001 ACS
RN **57-88-5** REGISTRY
CN Cholest-5-en-3-ol (3.beta.)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Cholesterol (8CI)
OTHER NAMES:
CN (-)-Cholesterol
CN .DELTA.5-Cholesten-3.beta.-ol
CN 3.beta.-Hydroxycholest-5-ene
CN 5:6-Cholesten-3.beta.-ol
CN Cholest-5-en-3.beta.-ol
CN Cholesterin
CN Cholesteryl alcohol
CN Dythol
CN Lidinit
CN Lidinite
CN Provitamin D
FS STEREOSEARCH
DR 209124-38-9, 218965-24-3
MF C27 H46 O
CI COM
LC STN Files: AGRICOLA, AIDSLINE, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DETHERM*, DIOGENES, DIPPR*, DRUGU, EMBASE, GMELIN*, HODOC*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PDLCOM*, PIRA, PROMT, RTECS*, SPECINFO, TOXLINE, TOXLIT, TULSA, ULIDAT, USAN, USPATFULL, VETU, VTB
(*File contains numerically searchable property data)

Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.



72923 REFERENCES IN FILE CA (1967 TO DATE)
7879 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
72997 REFERENCES IN FILE CAPLUS (1967 TO DATE)
15 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 135:13529

REFERENCE 2: 135:9934

REFERENCE 3: 135:9933

REFERENCE 4: 135:5228

REFERENCE 5: 135:4955

REFERENCE 6: 135:4954

REFERENCE 7: 135:4944

REFERENCE 8: 135:4943

REFERENCE 9: 135:4938

REFERENCE 10: 135:4934

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FILE COVERS 1947 - 23 Jun 2001 VOL 135 ISS 1
FILE LAST UPDATED: 22 Jun 2001 (20010622/ED)

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HCAplus now provides online access to patents and literature covered in CA from 1947 to the present. On April 22, 2001, bibliographic information and abstracts were added for over 2.2 million references published in CA from 1947 to 1966.

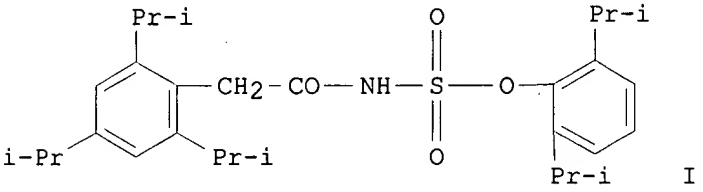
=> d l83 bib abs hitrn tot

L83 ANSWER 1 OF 13 HCAPLUS COPYRIGHT 2001 ACS
AN 2001:359777 HCAPLUS
DN 134:371771
TI Prevention of plaque rupture by **ACAT** inhibitors
IN Bocan, Thomas Michael Andrew
PA Warner-Lambert Company, USA
SO PCT Int. Appl., 108 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001034127	A1	20010517	WO 2000-US28705	20001017

W: AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, MZ, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 1999-163814 P 19991105
GI



I

AB This invention is the administration of an **ACAT** inhibitor to prevent monocyte-macrophage accumulation and MMP expression in atherosclerotic lesions. Further, this invention relates to methods of inhibiting destabilization and/or rupture of atherosclerotic plaques and treatment of unstable angina. Tablets were prepd. contg. a **ACAT** inhibitor such as I.

IT **9027-63-8**, Acyl coenzyme A-**cholesterol acyltransferase**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors; prevention of plaque rupture by **ACAT** inhibitors)

IT **202401-34-1**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (prevention of plaque rupture by **ACAT** inhibitors)

RE.CNT 15
RE
(1) Bocan; ARTERIOSCLER, THROMB, VASC BIOL 2000, V20(1), P70 HCAPLUS
(2) Bocan; ATHEROSCLEROSIS 1998, V139(1), P21 HCAPLUS
(5) Bocan, T; WO 0004892 A 2000 HCAPLUS
(6) Bocan, T; ARTERIOSCLEROSIS AND THROMBOSIS 1991, V11, P1830 HCAPLUS
(7) Erba Carlo Spa; GB 2280675 A 1995 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L83 ANSWER 2 OF 13 HCAPLUS COPYRIGHT 2001 ACS

AN 2000:190909 HCAPLUS
DN 132:231975
TI Tryptophanyl esters and their N-acyl derivatives for the prevention and treatment of diseases caused or exacerbated by oxidative processes
IN Behl, Christian; Moosmann, Bernd
PA Max-Planck-Gesellschaft zur Foerderung der Wissenschaften e.V., Germany
SO PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000015206	A2	20000323	WO 1999-EP6819	19990915
	WO 2000015206	A3	20000810		
	W: JP, US				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	DE 19842416	A1	20000413	DE 1998-19842416	19980916
PRAI	DE 1998-19842416	A	19980916		

AB Tryptophanyl esters or their N-acyl derivs. are useful for prophylaxis and treatment of oxidative pathol. processes in degenerative diseases and/or carcinomas. Preferred compds. are tryptophan octyl ester, N-oleoyltryptophan Et ester, and N-dodecanoyltryptophan Et ester. The compds. are used for treatment and/or prophylaxis of neurodegenerative diseases, cataracts, neoplastic diseases, and/or cardiovascular diseases, esp. for Alzheimer's disease, Parkinson's disease, stroke, amyotrophic lateral sclerosis, cancer, arteriosclerosis, and/or myocardial infarction. Thus, tryptophan octyl ester (.gtoreq.4 nM) protected human neuroblastoma cells in vitro from oxidative stress damage (160 .mu.M H2O2).
IT **261734-92-3 261734-93-4**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tryptophanyl esters and their N-acyl derivs. for prevention and treatment of diseases caused or exacerbated by oxidative processes)

L83 ANSWER 3 OF 13 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:214200 HCAPLUS
DN 129:402
TI Effects of F-1394, an **acyl-CoA:cholesterol acyltransferase** (**ACAT**) inhibitor, on **ACAT** activity in HepG2 cells and on hepatic secretion of lipids in triton WR-1339-induced hyperlipidemic rats: possible role of hepatic **ACAT** in very low density lipoprotein secretion
AU Aragane, Katsumi; Kusunoki, Jun; Kitamine, Tetsuya; Yamaura, Tetsuaki; Ohnishi, Haruo
CS Pharmaceuticals Research Laboratories, Fujirebio, Inc., Tokyo, 192, Japan
SO Jpn. J. Pharmacol. (1998), 76(3), 309-312
CODEN: JJPAAZ; ISSN: 0021-5198
PB Japanese Pharmacological Society
DT Journal
LA English
AB We examd. the inhibitory potency of F-1394 ((1S,2S)-2-[3-(2,2-dimethylpropyl)-3-nonylureido]cyclohexane-1-yl 3-[4R-N-(2,2,5,5-tetramethyl-1,3-dioxane-4-carbonyl)amino]propionate), an **acyl-CoA:cholesterol acyltransferase** (**ACAT**) inhibitor, on **ACAT** activity and its hypolipidemic effect. F-1394 inhibited whole-cell **ACAT** activity in HepG2 cells with an IC50 value of 42 nM. The potency of F-1394 was greater than that of the five other **ACAT** inhibitors tested (YM-17E, CI-976, 57-118, CL-277082 and DL-melinamide). In rats made hyperlipidemic by Triton WR-1339, F-1394 caused a redn. in the hepatic secretion rate of **cholesterol**. These data suggest that inhibition of hepatic **ACAT** activity helps to reduce very low d. lipoprotein secretion from the liver into the circulation.
IT **9027-63-8, Cholesterol acyltransferase**

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(F-1394 inhibition of hepatic **cholesterol acyltransferase** leading to redn. of very low d. lipoproteins in hypolipidemic mechanism).

IT **71806-22-9**
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(comparison with; F-1394 inhibition of hepatic **cholesterol acyltransferase** leading to redn. of very low d. lipoproteins in hypolipidemic mechanism)

L83 ANSWER 4 OF 13 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:262611 HCAPLUS
DN 126:297659
TI Use of non-absorbable synthetic **sulfated polysaccharides** to decrease **cholesterol** absorption
IN **Lange, Louis G. , III; Spilburg, Curtis A.**
PA Lange, Louis G., III, USA; Spilburg; Curtis A.
SO U.S., 20 pp. Cont. of U.S. Ser. No. 773,875, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 5616570	A	19970401	US 1994-283723	19940801 <--
PRAI US 1991-773875		19911018 <--		

AB This invention encompasses a method and compns. which inhibit pancreatic **cholesterol esterase** and triglyceride lipase and hence, lower **cholesterol** and triglycerides in the blood stream. **Sulfated** pectin was tested for **cholesterol esterase** inhibition and it had an IC50 of 0.6 mg/mL or 3.0 nM (assuming a mol. wt. of 200 kDa); importantly, native, **unsulfated** pectin did not inhibit **cholesterol esterase,** demonstrating the importance of **sulfation** for effective inhibition.

IT **75330-75-5, Lovastatin**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as addnl. agent; nonabsorbable synthetic **sulfated polysaccharides** to decrease **cholesterol** absorption)

IT **9026-00-0, Cholesterol esterase**
9027-63-8, Cholesterol acyl transferase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; nonabsorbable synthetic **sulfated polysaccharides** to decrease **cholesterol** absorption)

IT **1398-62-5, Chitin sulfate 9012-77-5**
9032-43-3, Cellulose sulfate 9042-14-2
, Dextran sulfate 9047-13-6,
Amylopectin sulfate 9049-31-4, Alginic acid sulfate 37293-26-8, Chitosan sulfate 65589-58-4
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nonabsorbable synthetic **sulfated polysaccharides** to decrease **cholesterol** absorption)

IT **9005-38-3**, Sodium alginate
RL: RCT (Reactant)
(prepn. of **sulfated** alginate; nonabsorbable synthetic **sulfated polysaccharides** to decrease **cholesterol** absorption)

L83 ANSWER 5 OF 13 HCAPLUS COPYRIGHT 2001 ACS
AN 1996:452005 HCAPLUS
DN 125:96066

TI Non-absorbable synthetic **sulfated** polysaccharides
IN **Lange, Louis G., III; Spilburg, Curtis A.; Reardan, Dayton T.**
PA Cv Therapeutics, Inc., USA
SO Eur. Pat. Appl., 25 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 712864	A2	19960522	EP 1995-307295	19951013 <--
	EP 712864	A3	19961016		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	US 5521303	A	19960528	US 1994-322782	19941013 <--
	CA 2160440	AA	19960414	CA 1995-2160440	19951012 <--
	CA 2160440	C	19980825		
	AU 9534240	A1	19960426	AU 1995-34240	19951012 <--
	AU 682792	B2	19971016		
	JP 08253502	A2	19961001	JP 1995-265885	19951013 <--
PRAI	US 1994-322782		19941013 <--		
	US 1995-451563		19950526		

AB This invention encompasses methods for manufg. purified, high mol. wt. **sulfated** polysaccharide compns. that inhibit pancreatic **cholesterol esterase** and lower cholesterol in the blood stream.
IT **9026-00-0, Cholesterol esterase**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors; nonabsorbable synthetic **sulfated** polysaccharides for lowering blood cholesterol)
IT **57-88-5**, Cholesterol, biological studies
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BIOL (Biological study); PROC (Process)
(nonabsorbable synthetic **sulfated** polysaccharides for lowering blood cholesterol)
IT **9032-43-3P, Cellulose sulfate**
RL: IMF (Industrial manufacture); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(nonabsorbable synthetic **sulfated** polysaccharides for lowering blood cholesterol)
IT **9004-34-6**, Cellulose, reactions
RL: PEP (Physical, engineering or chemical process); RCT (Reactant); PROC (Process)
(nonabsorbable synthetic **sulfated** polysaccharides for lowering blood cholesterol)

L83 ANSWER 6 OF 13 HCAPLUS COPYRIGHT 2001 ACS
AN 1995:735432 HCAPLUS
DN 123:102789
TI Methods and reagents for inhibiting cholesterol absorption in humans mediated by pancreatic **cholesterol esterase**
IN **Lange, Louis G., III**; Bosner, Matthew S.
PA CV Therapeutics, Inc., USA
SO Can. Pat. Appl., 15 pp.
CODEN: CPXXEB
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	CA 2127230	AA	19950102	CA 1994-2127230	19940630 <--
	AU 9466101	A1	19950112	AU 1994-66101	19940630 <--
	EP 640620	A2	19950301	EP 1994-304793	19940630 <--
	EP 640620	A3	19951129		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	JP 07165794	A2	19950627	JP 1994-151284	19940701 <--

PRAI US 1993-86517 19930701 <--
AB This invention relates to the human enzyme, pancreatic **cholesterol esterase** (PCE), and a receptor (PCER) for this protein expressed by cells of the intestinal lining. Specifically, the invention relates to the use of inhibitors of binding between PCE and PCER to reduce intestinal uptake of dietary cholesterol in humans. Antibodies, including antisera, and monoclonal and chimeric antibodies, and cell lines producing such antibodies, raised against the PCER protein or fragments or epitopes thereof, are also claimed. The invention also relates to the treatment of individuals with therapeutic drugs for the prevention or alleviation of disease states related to cholesterol metab.
IT **9026-00-0, Cholesterol esterase**
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(cholesterol-related diseases treatment with an inhibitor of pancreatic **cholesterol esterase** binding to its receptor)

L83 ANSWER 7 OF 13 HCAPLUS COPYRIGHT 2001 ACS
AN 1991:157212 HCAPLUS
DN 114:157212
TI The use of nonabsorbable synthetic **sulfated** polysaccharides to decrease cholesterol absorption
IN **Lange, Louis George, III; Spilburg, Curtis A.**
PA USA
SO PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9012579	A1	19901101	WO 1990-US2079	19900420	<--
	W: AU, CA, JP, US, US					
	RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE					
	US 5017565	A	19910521	US 1989-340868	19890420	<--
	US 5063210	A	19911105	US 1989-429398	19891031	<--
	CA 2053258	AA	19901021	CA 1990-2053258	19900420	<--
	CA 2053258	C	19980210			
	AU 9055356	A1	19901116	AU 1990-55356	19900420	<--
	AU 633569	B2	19930204			
	EP 469079	A1	19920205	EP 1990-907923	19900420	<--
	EP 469079	B1	19941207			
	R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE					
	JP 04503813	T2	19920709	JP 1990-506819	19900420	<--
	JP 08019001	B4	19960228			
	ES 2064736	T3	19950201	ES 1990-907923	19900420	<--
	US 5484777	A	19960116	US 1993-167725	19931215	<--

PRAI US 1989-340868 19890420 <--
US 1989-429398 19891031 <--
WO 1990-US2079 19900420 <--
US 1991-718280 19910620 <--
US 1992-928510 19920811 <--
AB A method and compns. for inhibiting pancreatic **cholesterol esterase** and triglyceride lipase are disclosed. These compns. decrease cholesterol and triglyceride levels in blood. Oral administration of nonabsorbable inhibitors of **cholesterol esterase** inhibit the intestinal absorption of cholesterol. The anticholesteremics are **sulfated** alginic acid, pectin, amylopectin, chitin, dextran, cellulose, agar, and chitosan.
IT **57-88-5**, Cholesterol, biological studies
RL: BIOL (Biological study)
(absorption of, by intestine, **sulfated** polysaccharide inhibition of)
IT **57-88-5**
RL: BIOL (Biological study)
(anticholesteremics and Hypolipemics, **cholesterol esterase** inhibiting **sulfated** polysaccharides as)

IT **1398-61-4D**, Chitin, **sulfated 9000-69-5D**, Pectin, **sulfated 9002-18-0D**, Agar, **sulfated 9004-34-6D**, Cellulose, **sulfated**, biological studies **9004-54-0D**, Dextran, **sulfated**, biological studies **9005-32-7D**, Alginic acid, **sulfated 9012-76-4D**, Chitosan, **sulfated 9037-22-3D**, Amylopectin, **sulfated**
RL: BIOL (Biological study)
(cholesterol absorption inhibition by)

IT **9027-63-8**
RL: BIOL (Biological study)
(inhibitors of, **sulfated** polysaccharides and, in treatment of hypercholesteremia)

IT **9026-00-0, Cholesterol esterase**
RL: BIOL (Biological study)
(inhibitors of, **sulfated** polysaccharides as, in treatment of hypercholesteremia)

L83 ANSWER 8 OF 13 HCAPLUS COPYRIGHT 2001 ACS
AN 1990:112089 HCAPLUS
DN 112:112089
TI Inhibition of intestinal cholesterol and fatty acid absorption with heparin or related substances
IN **Lange, Louis G., III; Spilburg, Curtis A.**; Kinnunen, Paula M.
PA Jewish Hospital of St. Louis, USA
SO PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 8908456	A1	19890921	WO 1989-US787	19890227 <--
	W: AU, JP				
	RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
	AU 8934348	A1	19891005	AU 1989-34348	19890227 <--
	US 5352601	A	19941004	US 1992-936103	19920826 <--
	US 5429937	A	19950704	US 1994-311862	19940926 <--
	US 5492822	A	19960220	US 1995-386433	19950210 <--
PRAI	US 1988-168424		19880315 <--		
	US 1989-312255		19890222 <--		
	WO 1989-US787		19890227 <--		
	US 1990-544212		19900626 <--		
	US 1991-655289		19910214 <--		
	US 1992-936103		19920826 <--		
	US 1994-311862		19940926 <--		

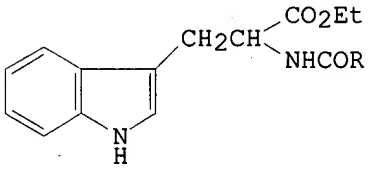
AB A method for inhibiting intestinal cell endogenous heparin-mediated absorption of cholesterol or fatty acids in mammals comprises orally administering to a mammal an effective amt. (5 mg-1g/day) of heparin, an active heparin subfraction, or heparinase. The fatty acids are those derived from the hydrolysis of cholesterol esters or triglycerides. Thus, male New Zealand white rabbits (1 kg) were fed 2% cholesterol Purina Rabbit Chow for two weeks plus either tap water or oral heparin (2 mg/mL) for 48 h prior to the expt. On day 15, the heparin-pretreated rabbits received 100 mg heparin in 10 mL water followed by 10 mL of radiolabeled liq. rabbit Chow contg. 50 .mu.Ci of [1,2,6,7-3H]cholesteryl oleate and the control group received 10 mL H2O followed by 10 mL of the same radiolabeled Chow. Compared to the control group, the heparin-treated group had 30% less 3H-cholesterol/cholesterol esters per mL of blood and 50% less per g of liver.

IT **57-88-5**, Cholesterol, biological studies
RL: BIOL (Biological study)
(absorption of, endogenous heparin-mediated, by intestine, inhibition of, with heparin or heparinase)

IT **9005-49-6**, Heparin, biological studies

RL: BIOL (Biological study)
(cholesterol and fatty acid absorption by intestine inhibition with)
IT **57-88-5D**, Cholesterol, esters
RL: BIOL (Biological study)
(fatty acids from, absorption of, by intestine, heparin or heparinase inhibition of)
IT **9026-00-0, Cholesterol esterase**
RL: PRP (Properties)
(interaction of, with heparin, in heparin or heparinase inhibition of endogenous heparin-mediated cholesterol absorption by intestine)

L83 ANSWER 9 OF 13 HCAPLUS COPYRIGHT 2001 ACS
AN 1985:89686 HCAPLUS
DN 102:89686
TI Relative absorption of tryptophan ethyl ester amide derivatives with various fatty acid chains in the dog
AU Tse, Francis L. S.; Christiano, Juliet R.; Talbot, Kenrick C.
CS Drug Metab. Sect., Sandoz, Inc., East Hanover, NJ, 07936, USA
SO J. Pharm. Pharmacol. (**1984**), 36(9), 633-6
CODEN: JPPMAB; ISSN: 0022-3573
DT Journal
LA English
GI



I

AB Sandoz compd. 57-118 is a mixt. of tryptophan Et ester amides (I, R = oleic, elaidic, linoleic, stearic, or palmitic acid moiety). The relative absorption of each of the 5 analogs was investigated in the dog following single oral doses of the homologous mixt. contg. 1 14C-labeled analog. It was shown that the extent of absorption of I (R = oleic acid) and its trans-isomer I (R = elaidic acid) were similar. An addnl. double bond in the fatty acid moiety (I, R = linoleic acid) facilitated gastrointestinal absorption. On the other hand, satd. fatty acid chains appeared to render the mols. less efficiently absorbed; the extent of absorption being dependent on the chain length. Thus, I (R = palmitic acid) with 16 carbon atoms on the fatty acid chain was better absorbed than I (R = stearic acid).
IT **71806-22-9 94921-32-1**
RL: BIOL (Biological study)
(absorption of, by intestine, fatty acid chain length and satn. in relation to)

L83 ANSWER 10 OF 13 HCAPLUS COPYRIGHT 2001 ACS
AN 1984:552341 HCAPLUS
DN 101:152341
TI N-Unsaturated fatty acid amides of tryptophan ester homologs and **anticholesteric** use thereof
IN Kathawala, Faizulla G.; Heider, John G.
PA Sandoz, Inc., USA
SO U.S., 9 pp. Cont.-in-part of U.S. Ser. No. 5,355, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 4
PATENT NO. KIND DATE APPLICATION NO. DATE

PI	US 4448785	A	19840515	US 1982-391548	19820624	<--
	BE 873365	A1	19790709	BE 1979-9228	19790109	<--
	ZA 7900087	A	19800827	ZA 1979-87	19790109	<--
PRAI	US 1978-867813		19780109	<--		
	US 1979-5355		19790122	<--		
	US 1978-867824		19780109	<--		
	US 1978-872836		19780127	<--		
	US 1978-881780		19780227	<--		
	US 1978-881781		19780227	<--		
	US 1978-891298		19780329	<--		
	BE 1979-1009228		19790109	<--		

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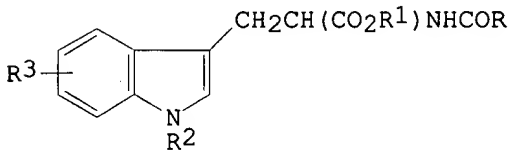
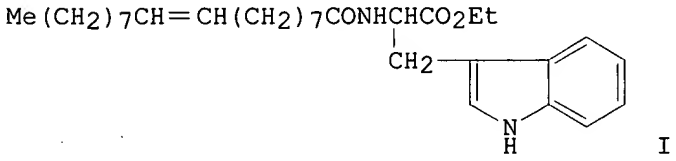


I

AB **Anticholesteremic** tryptophans I (RCO = unsatd. long-chain fatty acyl; R1 = alkyl, benzyl; R2 = H, alkyl, benzyl; R3 = H, halo, alkyl, alkoxy) were prepd. by N-acylation of tryptophan esters. Thus, linoleic acid was treated with ClCO2Et in CH2Cl2 contg. Et3N and the resulting mixed anhydride condensed with DL-Trp-OEt.HCl to give I (RCO = linoleoyl, R1 = Et, R2 = R3 = H) (II). At 10 mg/mL II inhibited 59-69% the accumulation of **cholesterol** ester in Fu5AH cells.

IT **71806-22-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

L83 ANSWER 11 OF 13 HCAPLUS COPYRIGHT 2001 ACS
AN 1984:45116 HCAPLUS
DN 100:45116
TI Role of **acyl CoA:cholesterol acyltransferase** in **cholesterol** absorption and its inhibition by 57-118 in the rabbit
AU **Heider, John G.**; Pickens, Carolyn E.; Kelly, Lawrence A.
CS Sandoz, East Hanover, NJ, 07936, USA
SO J. Lipid Res. (**1983**), **24**(9), **1127**-34
CODEN: JLPRAW; ISSN: 0022-2275
DT Journal
LA English
GI



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AB Esterification of **cholesterol** in rabbit small intestine mucosal microsomes by **acyl CoA:cholesterol acyltransferase** (EC 2.3.1.26)(**ACAT**) [**9027-63-8**] and mucosal cytosol by **cholesterol esterase** (EC 3.1.1.13) was studied. Compd. 57-118 [N-(1-oxo-9-octadecenyl)-DL-tryptophan(Z)ethyl ester](I) [**71806-22-9**] an inhibitor of **cholesterol** absorption, inhibited in vitro **ACAT** in

mucosal microsomes at concns. of 2-20 nmol/0.5 mL incubation mixt., but had no effect on **cholesterol esterase** in the cytosol at similar concns. A kinetic anal. using a Lineweaver-Burk plot indicates that I acts as a competitive inhibitor of **ACAT**. An ex vivo study in the rabbit where I was given by gavage at a dose of 200 mg/kg also showed inhibition of **ACAT** but not of **cholesterol esterase**. High-performance liq. chromatog. detn. of I in various subcellular fractions demonstrated the presence of this substance after oral administration in concns. in mucosal microsomes equiv. to those required to show inhibition of **ACAT** in vitro. These data support the work of K. R. Norum et al. (1979) indicating that mucosal **ACAT** plays a significant role in **cholesterol** absorption.

IT **57-88-5**, biological studies
RL: BIOL (Biological study)
(absorption of, by intestine, compd. 57-118 effect on, **cholesterol acyltransferase** in relation to)

IT **71806-22-9**
RL: BIOL (Biological study)
(**cholesterol acyltransferase** of small intestine mucosa inhibition by)

IT **9027-63-8**
RL: PROC (Process)
(of small intestine mucosa, compd. 57-118 inhibition of)

L83 ANSWER 12 OF 13 HCAPLUS COPYRIGHT 2001 ACS
AN 1981:174880 HCAPLUS
DN 94:174880
TI Pharmaceutical long-chain fatty acid amides of tryptophan derivatives
IN Heider, John G.; Kathawala, Faizulla Gulamhusein
PA Sandoz-Patent-G.m.b.H., Fed. Rep. Ger.
SO Ger. Offen., 20 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	DE 3024739	A1	19810129	DE 1980-3024739	19800630	<--
	GB 2052985	A	19810204	GB 1980-22202	19800707	<--
	JP 56032457	A2	19810401	JP 1980-91828	19800707	<--
	FR 2460931	A1	19810130	FR 1980-15237	19800709	<--
	FR 2460931	B1	19830624			
PRAI	US 1979-55801		19790709	<--		

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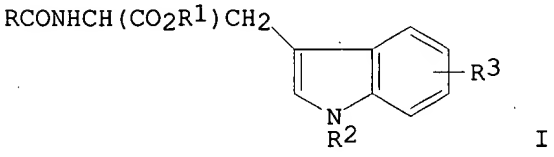

I

AB The **anticholesteremic** (no data) compds. I (R = C7-23 aliph. group contg. 1-4 double bonds or .alpha.,.beta.-methylene bridges; R1 = H, cation; R2 = H, C1-8 alkyl, PhCH2; R3 = H, F, Cl, Br, C1-3 alkyl or alkoxy) were prepd. Thus, I (RCO = oleyl, R1-R3 = H) was obtained by sapon. of the corresponding I (R1 = Et).

IT **71806-22-9**
RL: RCT (Reactant)
(sapon. of)

L83 ANSWER 13 OF 13 HCAPLUS COPYRIGHT 2001 ACS
AN 1979:593639 HCAPLUS

DN 91:193639
TI Fatty acid amide and hydrazide derivatives
IN Kathawala, Faizulla Gulamhusein; Heider, John G.
PA Sandoz-Patent-G.m.b.H., Switz.
SO Ger. Offen., 37 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	DE 2856856	A1	19790712	DE 1978-2856856	19781230	<--
	US 4229463	A	19801021	US 1978-881780	19780227	<--
	US 4194002	A	19800318	US 1978-891298	19780329	<--
	CH 644842	A	19840831	CH 1979-3	19790102	<--
	DK 7900030	A	19790710	DK 1979-30	19790103	<--
	FI 7900025	A	19790710	FI 1979-25	19790104	<--
	NL 7900084	A	19790711	NL 1979-84	19790105	<--
	GB 2012261	B2	19821222	GB 1979-337	19790105	<--
	GB 2012261	A	19790725			
	SE 7900142	A	19790710	SE 1979-142	19790108	<--
	SE 446093	B	19860811			
	SE 446093	C	19861120			
	JP 54109930	A2	19790829	JP 1979-138	19790108	<--
	JP 63023987	B4	19880518			
	ES 476648	A1	19791216	ES 1979-476648	19790108	<--
	CA 1101871	A1	19810526	CA 1979-319259	19790108	<--
	IL 56393	A1	19820831	IL 1979-56393	19790108	<--
	AT 7900118	A	19840615	AT 1979-118	19790108	<--
	AT 376962	B	19850125			
	BE 873365	A1	19790709	BE 1979-9228	19790109	<--
	AU 7943233	A1	19790719	AU 1979-43233	19790109	<--
	AU 529328	B2	19830602			
	FR 2416885	A1	19790907	FR 1979-438	19790109	<--
	FR 2416885	B1	19830422			
	ZA 7900087	A	19800827	ZA 1979-87	19790109	<--
	US 4185118	A	19800122	US 1979-2974	19790112	<--
	US 4248893	A	19810203	US 1979-9473	19790205	<--
	US 4201785	A	19800506	US 1979-27019	19790404	<--

PRAI US 1978-867813 19780109 <--
US 1978-867824 19780109 <--
US 1978-872836 19780127 <--
US 1978-881780 19780227 <--
US 1978-881781 19780227 <--
US 1978-891298 19780329 <--
DE 1978-2856856 19781230 <--
BE 1979-1009228 19790109 <--

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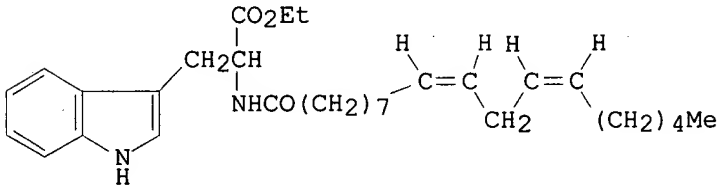

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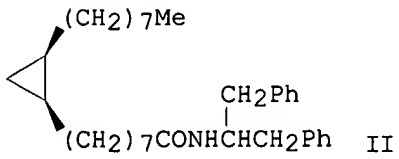

II

AB A wide range of title compds. (e.g., I, II) bearing unsatd. aliph. groups on the N atom(s) were prepd. as agents for combating arteriosclerosis by controlling blood **cholesterol** levels. Thus, linoleic acid, ClCO2Et, and (.+-.)-tryptophan Et ester-HCl gave I.
IT **71806-22-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

=> fil embase
FILE 'EMBASE' ENTERED AT 12:34:08 ON 23 JUN 2001

FILE COVERS 1974 TO 22 Jun 2001 (20010622/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d all tot

L148 ANSWER 1 OF 11 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
AN 94038358 EMBASE
DN 1994038358
TI Inhibition of inducible nitric oxide synthase in macrophages by oxidized low-density lipoproteins.
AU Yang X.; Cai B.; Sciacca R.R.; Cannon P.J.
CS Columbia University, 630 W 168th St,New York, NY 10032, United States
SO Circulation Research, (1994) 74/2 (318-328).
ISSN: 0009-7330 CODEN: CIRUAL
CY United States
DT Journal; Article
FS 018 Cardiovascular Diseases and Cardiovascular Surgery
029 Clinical Biochemistry
LA English
SL English
AB Uptake of oxidized low-density lipoprotein (LDL) by monocyte/macrophages to form 'foam' cells has been implicated in atherogenesis. Activated monocyte/macrophages synthesize nitric oxide (NO) from L-arginine. NO is cytotoxic, antiproliferative, and a vasodilator that inhibits platelet and monocyte adhesion. NO synthase mRNA, protein, and enzyme activity were induced in J774.A1 macrophages activated with **lipopolysaccharide** and gamma interferon. When macrophages were incubated with oxidized LDL for 24 hours and activated, there was a dose- and time-dependent inhibition of NO synthesis, assessed as nitrite accumulation in the media. When activated cells were incubated with nontoxic doses of lipoprotein (25 .mu.g/mL), neither native LDL nor acetyl LDL inhibited NO production, whereas oxidized LDL produced 50% inhibition. Levels of enzyme protein were unchanged by Western blot. Inhibition was a function of the degree of oxidation of LDL but was independent of **cholesteryl** esterification by the cells. Incubations of oxidized LDL with cells that had been pretreated with **dextran sulfate** or cytochalasin B yielded no evidence that inhibition was dependent on the scavenger receptor or directed endocytosis. Kinetic studies of inducible NO synthase from J774.A1 cells that were incubated with increasing doses of oxidized LDL indicated a pattern of noncompetitive inhibition. Inhibition of the enzyme was produced by lipids extracted from oxidized LDL but not by lipids extracted from native LDL. Because phosphatidylcholine (PC) is converted to lysophosphatidylcholine (LPC) during the oxidation of LDL, the effects of LPC were investigated. PC vesicles containing LPC did not inhibit enzyme activity but produced modest reductions in nitrite accumulation from cells. In contrast, PC vesicles had no significant effect. The data indicate that oxidized LDL lipid inhibits the activity of inducible NO synthase in activated macrophages. NO production by this enzyme and its inhibition by oxidized

LDL lipid may influence cell-to-cell interactions and vasomotor tone in atherosclerotic blood vessels.
CT Medical Descriptors:
*atherosclerosis
animal cell
article
cell stimulation
controlled study
enzyme activity
enzyme inhibition
lipid oxidation
macrophage activation
mouse
nonhuman
priority journal
Drug Descriptors:
***low density lipoprotein**
*nitric oxide synthase
RN (nitric oxide synthase) 125978-95-2

L148 ANSWER 2 OF 11 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
AN 92122604 EMBASE
DN 1992122604
TI Nutrition and therapeutics.
AU Nestel P.J.; Eisenberg S.
CS Australia
SO Current Opinion in Lipidology, (1992) 3/1 (1-4).
ISSN: 0957-9672 CODEN: COPLEU
CY United Kingdom
DT Journal; Editorial
FS 017 Public Health, Social Medicine and Epidemiology
018 Cardiovascular Diseases and Cardiovascular Surgery
029 Clinical Biochemistry
037 Drug Literature Index
038 Adverse Reactions Titles
LA English
CT Medical Descriptors:
***lipoprotein metabolism**
*nutrition
apheresis
atherosclerosis
bile acid metabolism
blood viscosity
cholesterol blood level
cholesterol metabolism
drug tolerance
drug use
editorial
erythrocyte aggregation
food composition
heart disease: PC, prevention
heart infarction prevention
human
human cell
hypercholesterolemia: TH, therapy
hyperlipidemia: DT, drug therapy
immunoadsorption
major clinical study
oxidation
patient selection
protein polymorphism
public health
side effect
treatment planning
Drug Descriptors:
acipimox: PD, pharmacology

antioxidant
apolipoprotein: EC, endogenous compound
apolipoprotein e: EC, endogenous compound
beta carotene
bezafibrate
bile acid: EC, endogenous compound
cholesterol: EC, endogenous compound
cholesterol acyltransferase: EC, endogenous compound
dextran sulfate
enzyme inhibitor: DV, drug development
fenofibrate
fibric acid derivative: PD, pharmacology
fibric acid derivative: AE, adverse drug reaction
fibrinogen: EC, endogenous compound
fish oil
gemfibrozil
heparin
high density lipoprotein cholesterol: EC, endogenous compound
hydroxymethylglutaryl coenzyme a reductase inhibitor: CB, drug combination
hydroxymethylglutaryl coenzyme a reductase inhibitor: AE, adverse drug reaction
hydroxymethylglutaryl coenzyme a reductase inhibitor: PD, pharmacology
linoleic acid
low density lipoprotein cholesterol: EC, endogenous compound
mevinolin
nicotinic acid: DT, drug therapy
nicotinic acid: DV, drug development
polyunsaturated fatty acid
pravastatin
probucol: DT, drug therapy
probucol: DV, drug development
simvastatin

RN (acipimox) 51037-30-0; (beta carotene) 7235-40-7; (bezafibrate) 41859-67-0; (**cholesterol**) **57-88-5**; (**cholesterol acyltransferase**) **9027-63-8**; (**dextran sulfate**) 9011-18-1, **9042-14-2**; (fenofibrate) 49562-28-9; (fibrinogen) 9001-32-5; (fish oil) 8016-13-5; (gemfibrozil) 25812-30-0; (heparin) 37187-54-5, 8057-48-5, 8065-01-8, 9005-48-5; (linoleic acid) 1509-85-9, 2197-37-7, 60-33-3, 822-17-3; (**mevinolin**) **75330-75-5**; (nicotinic acid) 54-86-4, 59-67-6; (pravastatin) 81131-74-0; (probucol) 23288-49-5; (simvastatin) 79902-63-9

L148 ANSWER 3 OF 11 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
AN 89050064 EMBASE
DN 1989050064
TI Regulation of 12-hydroxyeicosatetraenoic acid synthesis by acetyl-LDL in mouse peritoneal macrophages.
AU Mathur S.N.; Albright E.; Field F.J.
CS Department of Internal Medicine, University of Iowa, Iowa City, IA 52242, United States
SO Biochimica et Biophysica Acta - Lipids and Lipid Metabolism, (1989) 1001/1 (50-59).
ISSN: 0005-2760 CODEN: BBLLA6
CY Netherlands
DT Journal
FS 029 Clinical Biochemistry
LA English
SL English
AB The mechanism for the regulation of 12-hydroxyeicosatetraenoic acid (12-HETE) production by **cholesterol**-rich macrophages was investigated. .beta.-VLDL and acetyl-LDL, lipoproteins which result in **cholesterol** accumulation in macrophages, stimulated 12-HETE secretion. Lipoproteins which do not induce **cholesterol** accumulation, such as low- and high-density lipoproteins, did not.

Cell-free homogenates from **cholesterol**-rich macrophages had significantly more 12-lipoxygenase activity than homogenates from unmodified cells. Preincubating homogenates prepared from unmodified macrophages with acetyl-LDL, LDL or multilamellar liposomes containing total lipids from acetyl-LDL but not apoproteins significantly increased 12-lipoxygenase activity. This stimulatory effect was caused by the phospholipid moiety of the lipoprotein. 12-HETE synthesis was not increased in macrophages enriched 6-fold in unesterified **cholesterol**. Acetyl-LDL stimulated 12-HETE synthesis in macrophages in which **cholesteryl** ester accumulation was prevented by inhibiting acylcoenzyme A: **cholesterol acyltransferase** activity. When binding of acetyl-LDL to its receptor was decreased by increasing concentrations of **dextrans sulfate**, or when lysosomal metabolism of the lipoprotein was prevented by chloroquine, 12-HETE production significantly decreased. Moreover, the **combination** of inhibiting acetyl-LDL binding and degradation completely blocked the stimulation of 12-HETE synthesis by acetyl-LDL. The data indicate that acetyl-LDL must enter the macrophage and be partially degraded to regulate 12-HETE synthesis. The regulation is independent of **cholesterol** accumulation but is related to the entering lipoprotein phospholipid.

CT Medical Descriptors:
***cholesterol acetyltransferase**
mouse
animal cell
nonhuman
priority journal
Drug Descriptors:
*12 hydroxyicosatetraenoic acid
*arachidonate 12 lipoxygenase
***cholesterol**
***low density lipoprotein**
*phospholipid
***very low density lipoprotein**
radioisotope

RN (12 hydroxyicosatetraenoic acid) 54397-83-0, 59985-28-3, 71030-37-0; (arachidonate 12 lipoxygenase) 82391-43-3; (**cholesterol**) **57-88-5**

L148 ANSWER 4 OF 11 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
AN 84089976 EMBASE
DN 1984089976
TI The interaction of human apoB-containing lipoproteins with mouse peritoneal macrophages: A comparison of Lp(a) with LDL.
AU Krempler F.; Kostner G.M.; Roscher A.; et al.
CS First Department of Medicine, Landeskrankenanstalten, A-5020 Salzburg, Austria
SO Journal of Lipid Research, (1984) 25/3 (283-287).
CODEN: JLPRAW
CY United States
DT Journal
FS 029 Clinical Biochemistry
018 Cardiovascular Diseases and Cardiovascular Surgery
023 Nuclear Medicine
LA English
AB **Cholesteryl** ester accumulation in macrophages and foam cell formation is believed to play an important role in atherogenesis. The effect of Lp(a) on the incorporation of [14C]oleate into **cholesteryl** esters was studied in mouse peritoneal macrophages. In view of the physico-chemical similarities between Lp(a) and LDL, the results were compared with those obtained with LDL. Native Lp(a) and LDL did not stimulate **cholesteryl** ester formation. Incubation of macrophages with Lp(a)- or LDL-**dextran sulfate** complexes caused a significant increase in **cholesteryl** ester formation. A similar effect was observed when Lp(a) or LDL were incubated with macrophages in the presence of antibodies directed against the

specific Lp(a) apoprotein or against LpB. Treatment of Lp(a) with acetic anhydride or malondialdehyde (MDA) was followed by precipitation of most of the lipoprotein. Therefore, these modifications were not suitable to study the uptake of modified Lp(a) by macrophages. Studies with acetyl-LDL or MDA-treated LDL caused the well-known stimulation of [14C]oleate incorporation into **cholesteryl** esters. Thus, the modification of Lp(a) by **sulfated polysaccharides** or by treatment with antibodies yields similar **cholesteryl** ester deposition in mouse peritoneal macrophages as observed with modified LDL. This might be one mechanism by which Lp(a) exerts its atherogenicity.

CT Medical Descriptors:
oleic acid c 14
peritoneum macrophage
etiology
animal cell
nonhuman
mouse
peritoneum
Drug Descriptors:
***apolipoprotein b**
***lipoprotein**
***lipoprotein a**
***low density lipoprotein**
cholesterol ester
radioisotope

L148 ANSWER 5 OF 11 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
AN 83041541 EMBASE
DN 1983041541
TI Distribution of lecithin-**cholesterol acyltransferase** (LCAT) in human plasma lipoprotein fractions. Evidence for the association of active LCAT with low density lipoproteins.
AU Chen C.H.; Albers J.J.
CS Dep. Med., Harborview Med. Cent., Univ. Washington Sch. Med., Seattle, WA 98195, United States
SO Biochemical and Biophysical Research Communications, (1982) 107/3 (1091-1096).
CODEN: BBRCA
CY United States
DT Journal
FS 029 Clinical Biochemistry
LA English
AB The distribution of lecithin-**cholesterol acyltransferase** (LCAT) in human plasma was assessed by measuring both LCAT mass and activity in plasma fractions separated by **sequential** flotation ultracentrifugation, single-spin gradient ultracentrifugation, **dextran sulfate**-Mg2+ precipitation or agarose gel filtration. Although most of the LCAT was found to be associated with the high density lipoprotein fraction, a small amount of active LCAT (approximately 1% of the plasma LCAT mass and activity) was consistently associated with the low density lipoprotein fraction. LCAT was not found in the very low density lipoprotein fraction. The LDL-associated LCAT may play an important role in the acylation of lysolecithin by lysolecithin acyltransferase activity of LCAT.
CT Medical Descriptors:
plasma
human cell
human
normal human
Drug Descriptors:
*phosphatidylcholine sterol acyltransferase
***lipoprotein**
***low density lipoprotein**
RN (phosphatidylcholine sterol acyltransferase) 9031-14-5

L148 ANSWER 6 OF 11 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

AN 82122285 EMBASE
DN 1982122285
TI Lymphocyte-conditioned medium protects human monocyte-macrophages from **cholesteryl** ester accumulation.
AU Fogelman A.M.; Seager J.; Haberland M.E.; et al.
CS Div. Cardiol., Dept. Med., Sch. Med., UCLA, Los Angeles, CA 90024, United States
SO Proceedings of the National Academy of Sciences of the United States of America, (1982) 79/3 I (922-926).
CODEN: PNASA6
CY United States
DT Journal
FS 029 Clinical Biochemistry
018 Cardiovascular Diseases and Cardiovascular Surgery
LA English
AB Exposure of human monocyte-macrophages to as little as 50 .mu.l of culture medium from lymphocytes stimulated by concanavalin A (Con A) resulted in a dramatic decrease in the activities of the low density lipoprotein (LDL) receptor pathway, the LDL-**dextran sulfate** pathway, and the scavenger receptor pathway. This effect was not seen when the monocyte-macrophages were exposed to culture medium from lymphocytes cultured without Con A or with Con A **together** with .alpha.-methyl mannoside or control medium without lymphocytes. The activity of 3-hydroxy-3-methylglutaryl-coenzyme A reductase also decreased in monocyte-macrophages exposed to culture medium from stimulated lymphocytes. **Acyl-CoA-cholesterol** O-**acyltransferase** activity, protein synthesis, protein content, phagocytosis of heat-killed yeast, and non-receptor-mediated endocytosis were not inhibited. Monocyte-macrophages exposed to malondialdehyde altered-LDL in the presence of stimulated lymphocyte culture medium accumulated substantially less **cholesteryl** esters than did cells in control medium. The authors propose that substances produced by stimulated lymphocytes may be useful in protecting macrophages from **cholesteryl** ester accumulation.
CT Medical Descriptors:
*lymphocyte
*macrophage
*monocyte
protein synthesis
human cell
normal human
blood and hemopoietic system
lymphatic system
Drug Descriptors:
***cholesterol ester**
cholesterol acyltransferase
hydroxymethylglutaryl coenzyme a reductase
low density lipoprotein
RN (**cholesterol acyltransferase**) **9027-63-8**;
(hydroxymethylglutaryl coenzyme a reductase) 37250-24-1

L148 ANSWER 7 OF 11 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
AN 82031845 EMBASE
DN 1982031845
TI **Cholesterol** synthesis and esterification in experimental xanthoma tissues.
AU Kodama H.; Nagao Y.; Arakawa K.; et al.
CS Dept. Dermatol., Okayama Univ. Med. Sch., Shikata, Okayama 700, Japan
SO Journal of Lipid Research, (1981) 22/7 (1033-1041).
CODEN: JLPRAW
CY United States
DT Journal
FS 029 Clinical Biochemistry
013 Dermatology and Venereology
018 Cardiovascular Diseases and Cardiovascular Surgery
LA English

AB We studied **cholesterol** metabolism in experimental xanthoma tissues which were induced by injection of high molecular weight sodium **dextran sulfate** into the dermis of **hypercholesterolemic** rabbits. Control studies were performed on dermal specimens of the **dextran sulfate**-injected site of normolipemic rabbits. **Cholesterol** accumulation was much greater in the **hypercholesterolemic** rabbit tissues than in the normolipemic rabbit tissues. Histiocytes and foam cells in such lesions had an ability to synthesize **cholesterol**. However, **cholesterol** synthesis was suppressed in the **cholesterol** -rich tissues of **hypercholesterolemic** rabbits. This suppression was obviously caused by the accumulation of **cholesterol** in the tissues which take up lipoprotein in **hypercholesterolemic** rabbits. On the other hand, esterification of **cholesterol** was greater in the **hypercholesterolemic** rabbit tissues than in the normolipemic rabbit tissues. **Cholesterol** was esterified more selectively with oleic acid than with palmitic acid. Therefore, **cholesteryl** oleate increased in the tissues **concomitantly** with the accumulation of **cholesteryl** esters. Fatty acids of serum origin rather than those synthesized in situ were more important in the esterification process. It was suggested that **cholesterol** esterification was mediated by acyl-coenzyme A:**cholesterol** **acyltransferase** and that lecithin:**cholesterol** **acyltransferase** contributed little to the process.

CT Medical Descriptors:
***cholesterol esterification**
***hypercholesterolemia**
*xanthoma
in vitro study
animal experiment
Drug Descriptors:
***cholesterol**
cholesterol acyltransferase

RN (**cholesterol**) **57-88-5**; (**cholesterol** **acyltransferase**) **9027-63-8**

L148 ANSWER 8 OF 11 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
AN 82006160 EMBASE
DN 1982006160
TI Observations on the pathogenesis of xanthoma.
AU Kodama H.; Arakawa K.; Nagao Y.; et al.
CS Dept. Dermatol., Okayama Med. Sch., Okayama, Japan
SO Nishinihon Journal of Dermatology, (1981) 43/4 (566-570).
CODEN: NNHIAN
CY Japan
DT Journal
FS 013 Dermatology and Venereology
LA Japanese
SL English

AB Our observations on the pathogenesis of xanthoma were reported. Direct immunofluorescence using anti-human .beta.-lipoprotein antibody indicated that human .beta.-lipoprotein was incorporated into foam cells of human xanthomas and an experimental rabbit xanthoma which was induced by human .beta.-lipoprotein immune complexes in the blood stream. Foam cells originate from scavenger cells, such as dermal histiocytes and not from fibroblasts. Histiocytes incorporate more readily denatured lipoproteins than lipoproteins of native form. **Cholesterol** metabolism was investigated in experimental xanthoma tissues which were induced by intradermal **dextran sulfate** injection.
Cholesterol synthesis was suppressed and **cholesterol** esterification was increased in the **cholesterol**-rich xanthoma tissues. **Cholesterol** was esterified more selectively with oleic acid than with palmitic acid. Therefore, **cholesterol** oleate increases in the tissues **concomitantly** with the accumulation of **cholesteryl** esters. The more important role in the esterification was played by the fatty acids of serum origin rather than those

synthesized in situ. These findings suggest that the **cholesterol** esterification was mediated by **acyl-CoA**: **cholesterol acyltransferase** and that lecithin: **cholesterol acyltransferase** had contributed little to the esterification.
CT Medical Descriptors:
*xanthoma
theoretical study
human cell
etiology
histology
cytology
Drug Descriptors:
***low density lipoprotein**
***cholesterol**
RN (**cholesterol**) **57-88-5**

L148 ANSWER 9 OF 11 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
AN 79110459 EMBASE
DN 1979110459
TI Binding site on macrophages that mediates uptake and degradation of acetylated low density lipoprotein, producing massive **cholesterol** deposition.
AU Goldstein J.L.; Ho Y.K.; Basu S.K.; Brown M.S.
CS Dept. Molec. Genet., Univ. Texas Hlth Sci. Cent., Dallas, Tex. 75235, United States
SO Proceedings of the National Academy of Sciences of the United States of America, (1979) 76/1 (333-337).
CODEN: PNASA6
CY United States
DT Journal
FS 029 Clinical Biochemistry
018 Cardiovascular Diseases and Cardiovascular Surgery
LA English
AB Resident mouse peritoneal macrophages were shown to take up and degrade acetylated 125I-labeled low density lipoprotein (125I-acetyl-LDL) in vitro at rates that were 20-fold greater than those for the uptake and degradation of 125I-LDL. The uptake of 125I-acetyl-LDL and its subsequent degradation in lysosomes were attributable to a high-affinity, trypsin-sensitive, surface binding site that recognized acetyl-LDL but not native LDL. When 125I-acetyl-LDL was bound to this site at 4.degree.C and the macrophages were subsequently warmed to 37.degree.C, 75% of the cell-bound radioactivity was degraded to mono[125I]iodotyrosine within 1 hr. The macrophage binding site also recognized maleylated LDL, maleylated albumin, and two **sulfated polysaccharides** (fucoidin and **dextran sulfate**) indicating that negative charges were important in the binding reaction. A similar binding site was present on rat peritoneal macrophages, guinea pig Kupffer cells, and cultured human mococytes but not on human lymphocytes or fibroblasts, mouse L cells or Y-1 adrenal cells, or Chinese hamster ovary cells. Uptake and degradation of acetyl-LDL via this binding site stimulated **cholesterol** esterification 100-fold and produced a 38-fold increase in the cellular content of **cholesterol** in mouse peritoneal macrophages. although the physiologic significance, if any, of this macrophage uptake mechanism is not yet known, we hypothesize that it may mediate the degradation of denatured LDL in the body and thus serve as a 'backup' mechanism for the previously described receptor-mediated degradation of native LDL that occurs in parenchymal cells. Such a scavenger pathway might account for the widespread deposition of LDL-derived **cholesteryl** esters in macrophages of patients with familial **hypercholesterolemia** in whom the parenchymal cell pathway for LDL degradation is blocked, owing to a genetic deficiency of receptors for native LDL.
CT Medical Descriptors:
in vitro study
animal experiment

mouse
peritoneum
Drug Descriptors:
***cholesterol**
***low density lipoprotein**
radioisotope
RN (**cholesterol**) **57-88-5**

L148 ANSWER 10 OF 11 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
AN 79095290 EMBASE
DN 1979095290
TI The influence of various lipoproteins and apolipoproteins on the in vitro esterification of **cholesterol** in human serum by the enzyme lecithin: **Cholesterol acyltransferase**.
AU Kostner G.M.
CS Inst. Med. Biochem., Univ. Graz, Austria
SO Scandinavian Journal of Clinical and Laboratory Investigation, (1978) 38/SUPPL. 150 (66-71).
CODEN: SJCLAY
CY Norway
DT Journal
FS 029 Clinical Biochemistry
003 Endocrinology
LA English
AB The influence of various lipoproteins, apolipoproteins, and lipoprotein lipids on the initial rate of **cholesterol** esterification (IRE) by the enzyme lecithin:**cholesterol acyltransferase** (LCAT) has been studied in vitro in sera from normolipemic and hyperlipemic human subjects. This was achieved by adding isolated lipoprotein density fractions and families to fresh sera, on the one hand, and by specific adsorption of distinct lipoprotein classes with antibodies and polyanions on the other. The results were as follows: (1) Addition of all known lipoprotein density classes to normal serum, except for HDL2, had no influence on the IRE but reflected to some degree the mode of assay system. Addition of HDL2 inhibited the LCAT and the inhibitor was chloroform methanol extractable. The addition of LpC, a minor fraction from HDL of all normal sera, markedly enhanced the IRE. (2) Removal of VLDL plus LDL by antibodies or **dextran sulfate** had little if any effect. After precipitation of all LpA with anti-AI, approximately 50% of the LCAT activity remained in the supernatant and was active even in the assays where only endogenous substrate was provided. In the precipitated LpA the rest of the activity was found, despite the fact that antigenic determinants of apoAI were blocked by antibodies. The removal of LpC from the HDL-class was followed by a complete abolishment of LCAT activity. This activity, however, could partly be restored by adding exogenous substrate. (3) The IRE was found to be increased in persons with primary and post-prandial hypertriglyceridemia. In these cases the concentration of the LpC in HDL was also increased. These findings suggest that LpC of HDL plays a major role in the esterification of **cholesterol** in human serum under physiological conditions.
CT Medical Descriptors:
human cell
normal human
blood and hemopoietic system
Drug Descriptors:
***apolipoprotein**
*phosphatidylcholine sterol acyltransferase
***lipoprotein**
RN (phosphatidylcholine sterol acyltransferase) 9031-14-5

L148 ANSWER 11 OF 11 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
AN 78218564 EMBASE
DN 1978218564
TI [Determination of lecithin-**cholesterol acyltransferase**. Studies on the precipitation of .beta.-lipoproteins by **dextran sulphate**].

DOSAGE DE LA LECITHINE-**CHOLESTEROL ACYLTRANSFERASE**.
INTERET DE LA PRECIPITATION DES .beta.-LIPOPROTEINES PAR LE SULFATE DE DEXTRANE.
AU Alcindor L.G.; Melin B.; Benhamou G.; Piot M.C.
CS Lab. Biochem., Fac. Med., Paris, France
SO Clinica Chimica Acta, (1977) 81/2 (177-182).
CODEN: CCATAR
CY Netherlands
DT Journal
FS 029 Clinical Biochemistry
LA English
AB Uncertainties in assays of lecithin-**cholesterol** **acyltransferase** (LCAT) are generally related to the degree of isotopic equilibrium obtained by rapid exchange of unesterified **cholesterol** between the different lipoproteins. A new method is presented based on the precipitation of serum .beta.-lipoprotein with **sulfated polysaccharides** prior to the LCAT determination. In the absence of .beta.-lipoproteins, more than 7% of serum free **cholesterol** is esterified in the first hour and the reaction rate is linear for about 2 hr. LCAT activities with normal serum expressed as **cholesterol** esterified per .mu.mol/l/hr are lower than the values reported by others. The reason for this discrepancy is that free **cholesterol** specific activity in total serum does not reflect the true specific activity of LCAT **cholesterol** substrate.
CT Medical Descriptors:
in vitro study
theoretical study
normal human
Drug Descriptors:
***low density lipoprotein**
*phosphatidylcholine sterol acyltransferase
RN (phosphatidylcholine sterol acyltransferase) 9031-14-5

=> fil medline
FILE 'MEDLINE' ENTERED AT 13:12:16 ON 23 JUN 2001

FILE LAST UPDATED: 18 JUN 2001 (20010618/UP). FILE COVERS 1958 TO DATE.

On April 22, 2001, MEDLINE was reloaded. See HELP RLOAD for details.

MEDLINE now contains new records from the former NLM HEALTH STAR database. These records have an Entry Date and Update Date of 20010223.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2001 vocabulary. Enter HELP THESAURUS for details.

The OLDMEDLINE file segment now contains data from 1958 through 1965. Enter HELP CONTENT for details.

Left, right, and simultaneous left and right truncation are available in the Basic Index. See HELP SFIELDS for details.

THIS FILE CONTAINS CAS REGISTRY NUMBERS FOR EASY AND ACCURATE SUBSTANCE IDENTIFICATION.

=> d all tot l166

L166 ANSWER 1 OF 5 MEDLINE
AN 91141343 MEDLINE
DN **91141343** PubMed ID: **1899899**
TI Pravastatin and simvastatin for hypercholesterolemia.
AU Anonymous
SO MEDICAL LETTER ON DRUGS AND THERAPEUTICS, (1991 Mar 8) 33 (839) 18-20.
Journal code: M52; 2985240R. ISSN: 0025-732X.

CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199103
ED Entered STN: 19910412
Last Updated on STN: 19980206
Entered Medline: 19910327
CT Check Tags: Human
Anticholesteremic Agents: AE, adverse effects
*Anticholesteremic Agents: TU, therapeutic use
Clinical Trials
Drug Therapy, Combination
Heptanoic Acids: AE, adverse effects
*Heptanoic Acids: TU, therapeutic use
*Hypercholesterolemia: DT, drug therapy
Liver Diseases: CI, chemically induced
Lovastatin: AE, adverse effects
*Lovastatin: AA, analogs & derivatives
Lovastatin: TU, therapeutic use
Muscular Diseases: CI, chemically induced
Naphthalenes: AE, adverse effects
*Naphthalenes: TU, therapeutic use
Pravastatin
Simvastatin
RN 75330-75-5 (Lovastatin); 79902-63-9 (Simvastatin); 81093-37-0 (Pravastatin)
CN 0 (Anticholesteremic Agents); 0 (Heptanoic Acids); 0 (Naphthalenes)

L166 ANSWER 2 OF 5 MEDLINE
AN 90072254 MEDLINE
DN **90072254** PubMed ID: **2589420**
TI Controlling cholesterol with drugs.
AU Stoy D B
CS George Washington University Lipid Research Clinic, Washington, DC.
SO AMERICAN JOURNAL OF NURSING, (1989 Dec) 89 (12) 1628-31.
Journal code: 3MW; 0372646. ISSN: 0002-936X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Nursing Journals
EM 199001
ED Entered STN: 19900328
Last Updated on STN: 19900328
Entered Medline: 19900105
CT Check Tags: Human
*Anticholesteremic Agents: TU, therapeutic use
Cholestyramine: TU, therapeutic use
Drug Therapy, Combination
*Hypercholesterolemia: DT, drug therapy
Lovastatin: TU, therapeutic use
Niacin: TU, therapeutic use
RN 11041-12-6 (Cholestyramine); 59-67-6 (Niacin); 75330-75-5 (Lovastatin)
CN 0 (Anticholesteremic Agents)

L166 ANSWER 3 OF 5 MEDLINE
AN 88339119 MEDLINE
DN **88339119** PubMed ID: **3421570**
TI Lovastatin, nicotinic acid, and rhabdomyolysis.
AU Reaven P; Witztum J L
SO ANNALS OF INTERNAL MEDICINE, (1988 Oct 1) 109 (7) 597-8.
Journal code: 5A6; 0372351. ISSN: 0003-4819.
CY United States
DT Letter
LA English
FS Abridged Index Medicus Journals; Priority Journals

EM 198810
ED Entered STN: 19900308
Last Updated on STN: 19900308
Entered Medline: 19881025
CT Check Tags: Case Report; Human; Male
Adult
Drug Therapy, Combination
Hypercholesterolemia, Familial: DT, drug therapy
*Lovastatin: AE, adverse effects
*Niacin: AE, adverse effects
*Rhabdomyolysis: CI, chemically induced
RN 59-67-6 (Niacin); 75330-75-5 (Lovastatin)

L166 ANSWER 4 OF 5 MEDLINE
AN 88136074 MEDLINE
DN **88136074** PubMed ID: **3277742**
TI HMG-CoA reductase inhibitors. A new approach to the management of hypercholesterolemia.
AU Cressman M D; Hoogwerf B J; Moodie D S; Olin J W; Weinstein C E
SO CLEVELAND CLINIC JOURNAL OF MEDICINE, (1988 Jan-Feb) 55 (1) 93-100. Ref: 21
Journal code: DBN; 8703441. ISSN: 0891-1150.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 198804
ED Entered STN: 19900308
Last Updated on STN: 19900308
Entered Medline: 19880406
CT Check Tags: Human
Colestipol: TU, therapeutic use
Drug Therapy, Combination
*Hydroxymethylglutaryl CoA Reductases: AI, antagonists & inhibitors
*Hypercholesterolemia: DT, drug therapy
Lovastatin: AE, adverse effects
*Lovastatin: TU, therapeutic use
RN 50925-79-6 (Colestipol); 75330-75-5 (Lovastatin)
CN EC 1.1.1.88 (Hydroxymethylglutaryl CoA Reductases)

L166 ANSWER 5 OF 5 MEDLINE
AN 88125202 MEDLINE
DN **88125202** PubMed ID: **3340642**
TI Lovastatin alone and in combination for treatment of primary hypercholesterolemia.
AU Stein E A; Lamkin G E; Bewley D Z
CS Cholesterol Treatment Center, University of Cincinnati Medical Center, Ohio 45267-0714.
SO PROGRESS IN CLINICAL AND BIOLOGICAL RESEARCH, (1988) 255 281-93.
Journal code: PZ5; 7605701. ISSN: 0361-7742.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198803
ED Entered STN: 19900308
Last Updated on STN: 19900308
Entered Medline: 19880323
CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't
Adult
Aged
Anion Exchange Resins: TU, therapeutic use
Drug Therapy, Combination
*Hypercholesterolemia: DT, drug therapy

Hypercholesterolemia, Familial: DT, drug therapy
Lipoproteins, HDL Cholesterol: BL, blood
Lipoproteins, LDL Cholesterol: BL, blood
Lovastatin: AE, adverse effects
*Lovastatin: TU, therapeutic use
Middle Age
Niacin: TU, therapeutic use
Patient Compliance
RN 59-67-6 (Niacin); 75330-75-5 (Lovastatin)
CN 0 (Anion Exchange Resins); 0 (Lipoproteins, HDL Cholesterol); 0 (Lipoproteins, LDL Cholesterol)

=> d all tot l173

L173 ANSWER 1 OF 63 MEDLINE
AN 95196837 MEDLINE
DN 95196837 PubMed ID: 7890014
TI The effect of probucol and vitamin E treatment on the oxidation of low-density lipoprotein and forearm vascular responses in humans.
AU McDowell I F; Brennan G M; McEneny J; Young I S; Nicholls D P; McVeigh G E; Bruce I; Trimble E R; Johnston G D
CS Department of Clinical Biochemistry, Queen's University, Royal Victoria Hospital, Belfast, Northern Ireland.
SO EUROPEAN JOURNAL OF CLINICAL INVESTIGATION, **(1994 Nov)** 24 (11) 759-65.
Journal code: EN3; 0245331. ISSN: 0014-2972.
CY ENGLAND: United Kingdom
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LA English
FS Priority Journals
EM 199504
ED Entered STN: 19950427
Last Updated on STN: 19980206
Entered Medline: 19950414
AB This study investigates the hypothesis that lipid soluble antioxidants may increase the resistance of low-density lipoprotein (LDL) to oxidation and also enhance vascular endothelial responses in humans. In a double-blind parallel group study, 24 **hypercholesterolaemic** patients already on treatment with simvastatin (20 mg day-1), were randomized to supplementary treatment with probucol (500 mg bd), vitamin E (400 IU daily) or placebo for 8 weeks. Mean serum **cholesterol** before antioxidant treatment was 7.00 mmol l-1. Resistance of LDL to oxidation by copper was increased by 830% in the probucol group and by 30% in the vitamin E group. However, thiobarbituric acid reacting substances in whole serum were not altered by either antioxidant. Probucol lowered HDL- and LDL-**cholesterol** levels and increased the QT interval. Forearm vascular responses, as measured by venous occlusion plethysmography, to acetylcholine, glyceryl trinitrate and NG-monomethyl-L-arginine, were not significantly changed by antioxidant treatment. Probucol has a major, and vitamin E a minor, effect on LDL resistance to oxidation but neither compound appears to alter forearm vascular responses in vivo.
CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't
Adult
Antilipemic Agents: AD, administration & dosage
Double-Blind Method
Drug Administration Schedule
Drug Therapy, Combination
*Forearm: BS, blood supply
Hyperlipidemia: BL, blood
***Hyperlipidemia: DT, drug therapy**
***Lipoproteins, LDL Cholesterol: BL, blood**
Lipoproteins, LDL Cholesterol: DE, drug effects
Lovastatin: AD, administration & dosage

Lovastatin: AA, analogs & derivatives
Middle Age
Oxidation-Reduction: DE, drug effects
***Probucol: AD, administration & dosage**
Probucol: AE, adverse effects
Regional Blood Flow
Simvastatin
*Vitamin E: AD, administration & dosage
Vitamin E: AE, adverse effects
Vitamin E: BL, blood
RN 1406-18-4 (Vitamin E); 23288-49-5 (Probucol); **75330-75-5 (Lovastatin)**; 79902-63-9 (Simvastatin)
CN 0 (Antilipemic Agents); 0 (Lipoproteins, LDL **Cholesterol**)

L173 ANSWER 2 OF 63 MEDLINE
AN 95181606 MEDLINE
DN 95181606 PubMed ID: 7876371
TI Dual bezafibrate-simvastatin therapy for combined hyperlipidaemia.
AU Hutchesson A C; Moran A; Jones A F
CS Department of Clinical Chemistry, Birmingham Heartlands Hospital, Bordesley Green East, U.K.
SO JOURNAL OF CLINICAL PHARMACY AND THERAPEUTICS, **(1994 Dec)** 19 (6) 387-9.
Journal code: HPI; 8704308. ISSN: 0269-4727.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199504
ED Entered STN: 19950419
Last Updated on STN: 19980206
Entered Medline: 19950406
AB Statins and fibrates are both effective in the treatment of hyperlipidaemias but are not recommended in combination because episodes of rhabdomyolysis have followed combined **lovastatin**-gemfibrozil therapy. We assessed treatment with dual bezafibrate-simvastatin therapy in routine clinical practice. In 22 patients, total **cholesterol**, LDL-**cholesterol** and triglycerides fell by 20.1% ($P < 0.0001$), 35.1% ($P < 0.001$) and 31% ($P < 0.05$) respectively, and HDL-**cholesterol** rose by 18.4% ($P < 0.05$) on combination therapy. The reduction in **cholesterol** followed the introduction of simvastatin, while the decrease in triglycerides followed treatment with bezafibrate. No patient developed myopathy. We conclude that dual simvastatin-bezafibrate therapy is well tolerated and may reduce triglyceride concentrations, but offers no advantage in **cholesterol** reduction over treatment with simvastatin alone.
CT Check Tags: Female; Human; Male
Adult
Aged
*Antilipemic Agents: TU, therapeutic use
***Bezafibrate: TU, therapeutic use**
Cholesterol: BL, blood
Drug Therapy, Combination
Hyperlipidemia: BL, blood
***Hyperlipidemia: DT, drug therapy**
Lipoproteins, HDL Cholesterol: BL, blood
Lipoproteins, LDL Cholesterol: BL, blood
***Lovastatin: AA, analogs & derivatives**
Lovastatin: TU, therapeutic use
Middle Age
Simvastatin
Triglycerides: BL, blood
RN 41859-67-0 (Bezafibrate); **57-88-5 (Cholesterol)**; **75330-75-5 (Lovastatin)**; 79902-63-9 (Simvastatin)
CN 0 (Antilipemic Agents); 0 (Lipoproteins, HDL **Cholesterol**); 0 (Lipoproteins, LDL **Cholesterol**); 0 (Triglycerides)

L173 ANSWER 3 OF 63 MEDLINE
AN 95171622 MEDLINE
DN 95171622 PubMed ID: 7867225
TI HBPRCA Astra Award. Therapeutic restoration of endothelial function in **hypercholesterolaemic** subjects: effect of fish oils.
AU Chin J P; Dart A M
CS Alfred and Baker Medical Unit, Baker Medical Research Institute, Prahan, Victoria, Australia.
SO CLINICAL AND EXPERIMENTAL PHARMACOLOGY AND PHYSIOLOGY, **(1994 Oct)** 21 (10) 749-55.
Journal code: DD8; 0425076. ISSN: 0305-1870.
CY Australia
DT (CLINICAL TRIAL)
(CONTROLLED CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199503
ED Entered STN: 19950407
Last Updated on STN: 19980206
Entered Medline: 19950329
AB 1. Endothelial dysfunction, evidenced as an impaired response to acetylcholine, is well documented in **hypercholesterolaemic** subjects. We examined the ability of dietary supplementation with fish oils to restore endothelial function in forearm resistance vessels in these patients and compared this with restoration by lipid-lowering therapy. 2. Responses of forearm blood flow to acetylcholine (4.6, 9.25, 18.5 and 37 micrograms/min) and sodium nitroprusside (200, 400, 800 and 1600 ng/min) were obtained using forearm venous occlusion plethysmography in nine **hypercholesterolaemic** and seven age-matched control subjects. The dose-response curve to acetylcholine was significantly blunted in **hypercholesterolaemic** subjects when compared with controls ($P < 0.001$). Responses to sodium nitroprusside were not different between the two groups ($P = 0.37$). 3. Lipid-lowering therapy decreased total plasma **cholesterol** levels by 33% and significantly augmented the responses to acetylcholine ($P = 0.001$) but not to sodium nitroprusside in the **hypercholesterolaemic** subjects. 4. Dietary supplementation with fish oils had no effect on either total or low density lipoprotein-**cholesterol** but significantly augmented the responses to acetylcholine ($P = 0.011$) in **hypercholesterolaemic** subjects. Responses to sodium nitroprusside were not altered ($P = 0.94$). 5. This study shows that endothelium-dependent relaxation is impaired in subjects with high **cholesterol** levels and that this impairment can be reversed by lowering low density lipoproteins (LDL) **cholesterol** levels. In addition, we demonstrate that restoration of endothelial function can occur without changes in LDL levels, by dietary supplementation with fish oils.
CT Check Tags: Female; Human; Male
Acetylcholine: PD, pharmacology
Adult
Australia
Awards and Prizes
Cholesterol: BL, blood
Cholestyramine: TU, therapeutic use
Drug Therapy, Combination
*Endothelium, Vascular: DE, drug effects
*Fish Oils: TU, therapeutic use
Forearm: BS, blood supply
***Hypercholesterolemia: DH, diet therapy**
Hypertension
Lipoproteins, LDL Cholesterol: BL, blood
Lovastatin: AA, analogs & derivatives
Lovastatin: TU, therapeutic use
Middle Age
Regional Blood Flow: DE, drug effects

Simvastatin
RN **11041-12-6 (Cholestyramine)**; 51-84-3 (Acetylcholine); **57-88-5 (Cholesterol)**; **75330-75-5 (Lovastatin)**; 79902-63-9 (Simvastatin)
CN 0 (Fish Oils); 0 (Lipoproteins, LDL **Cholesterol**)

L173 ANSWER 4 OF 63 MEDLINE
AN 95154373 MEDLINE
DN 95154373 PubMed ID: 7851467
TI Postprandial apolipoprotein B100 and B48 metabolism in familial combined hyperlipidaemia before and after reduction of fasting plasma triglycerides.
AU Castro Cabezas M; Erkelens D W; Kock L A; De Bruin T W
CS Department of Internal Medicine, University Hospital, Utrecht, The Netherlands.
SO EUROPEAN JOURNAL OF CLINICAL INVESTIGATION, **(1994 Oct)** 24 (10) 669-78.
Journal code: EN3; 0245331. ISSN: 0014-2972.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199503
ED Entered STN: 19950322
Last Updated on STN: 19980206
Entered Medline: 19950313
AB Hepatic VLDL overproduction in familial combined hyperlipidaemia (FCH) may delay the clearance of atherogenic apolipoprotein (apo) B containing particles. We investigated if normalization of fasting plasma triglycerides (TG) by hypolipidaemic treatment results in improved metabolism of apo B48 and apo B100 in six male subjects with FCH and compared them to six normolipidaemic controls. The FCH patients were studied before (TG, 5.2 +/- 1.2 mmol l-1; mean +/- SEM) and after therapy (TG, 2.1 +/- 0.3 mmol l-1) with either simvastatin (n = 4) or combined therapy with gemfibrozil (n = 2). The postprandial changes of apo B100 and apo B48 were studied after a single oral fat meal (24 h; 50 gram fat m-2). Changes in triglyceride rich particles (TRP; d < 1.006 g ml-1) and remnant fractions (REM; d:1.006-1.019 g ml-1) of apo B were quantitated by scanning silverstained SDS-PAGE (4-15%). Apo B48 in fasting TRP in untreated and treated FCH was 15% and 14% of total apo B, and 6% in controls (P < 0.05). In controls, postprandial B48 increased maximally at 4 h by 81% in TRP and by 137% in REM compared to baseline. In treated FCH, the postprandial apo B48 pattern normalized in TRP compared to the untreated state. Postprandial apo B100 in controls decreased in TRP and REM by 33% and 18% (P < 0.05). In untreated and treated FCH, postprandial apo B100 remained unchanged vs. baseline in TRP and in REM suggesting hypersecretion of VLDL. The elimination of B100--assessed as area under the curve--in TRP (32.5 +/- 3.6 au.h; mean +/- SEM) and REM fractions (33.2 +/- 3.1 au.h), improved significantly after treatment (21.0 +/- 2.8 and 20.4 +/- 3.3 au.h, respectively). The apo B48 clearance in TRP fractions was improved after treatment (4.3 +/- 1.4 au.h vs. 2.9 +/- 1.2 au.h; P = 0.06), but not in REM fractions (2.8 +/- 1.0 au.h vs. 1.8 +/- 0.5 au.h; NS). In conclusion, in FCH subjects with apo B100 hypersecretion and increased fasting plasma apo B48 levels, reduction of fasting plasma TG improved, but did not normalize, TRP apo B48 and B100 metabolism. However, therapy normalized postprandial apo B100 remnant metabolism. Impaired postprandial apo B metabolism may be instrumental in the development of premature atherosclerosis in FCH subjects.
CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't
Adult
Aged
*Apolipoproteins B: ME, metabolism
Child
Cholesterol: BL, blood
Drug Therapy, Combination
Fasting

*Gemfibrozil: AD, administration & dosage
Hyperlipidemia, Familial Combined: BL, blood
Hyperlipidemia, Familial Combined: DT, drug therapy
***Hyperlipidemia, Familial Combined: ME, metabolism**
Lovastatin: AD, administration & dosage
***Lovastatin: AA, analogs & derivatives**
Middle Age
Simvastatin
*Triglycerides: BL, blood
RN 25812-30-0 (Gemfibrozil); **57-88-5 (Cholesterol)**; **75330-75-5 (Lovastatin)**; 79902-63-9 (Simvastatin)
CN 0 (Apolipoproteins B); 0 (Triglycerides); 0 (apolipoprotein B-100); 0 (apolipoprotein B-48)

L173 ANSWER 5 OF 63 MEDLINE
AN 95066045 MEDLINE
DN 95066045 PubMed ID: 7975581
TI [Effect of combined treatment with **lovastatin** and colestipol on serum lipids and lipoproteins].
Wplyw skojarzonego leczenia **lovastatinem** i kolestipolem na lipidy i lipoproteiny surowicy.
AU Klosiewicz-Latoszek L; Nowicka G; Szostak W B
CS Zakladu Zywienia Kliniczego Instytutu Zywnosci i Zywienia w Warszawie.
SO WIADOMOSCI LEKARSKIE, **(1993 Aug)** 46 (15-16) 581-5.
Journal code: XOA; 9705467. ISSN: 0043-5147.
CY Poland
DT Journal; Article; (JOURNAL ARTICLE)
LA Polish
FS Priority Journals
EM 199412
ED Entered STN: 19950110
Last Updated on STN: 19950110
Entered Medline: 19941215
AB In 20 men with **hypercholesterolaemia** or mixed hyperlipaemia the effect was evaluated of treatment with **Lovastatin** and Colestipol on lipoproteins. Administration of the drugs in combination or alone decreased significantly the concentrations of total **cholesterol** (TC), LDL **cholesterol** (LDL-chol), and apolipoprotein B (apo B). The combination of **Lovastatin** in dose of 40 mg with Colestipol in dose of 10 g decreased more favourably the concentrations of TC (34.7%), LDL-chol (44.3%), and apo B (22.4%) than administration of each of the drugs alone in higher doses i.e. **Lovastatin** 80 mg (TC--26.8%, LDL-chol--31.8%, apo B--16.9%) or Colestipol 20 g (TC -20.0%, LDL-chol-26.3%, apo B-10.8%). The treatment with **Lovastatin** and Colestipol failed to change significantly the concentrations of triglycerides, HDL **cholesterol** and AI and AII apolipoproteins. The combined therapy was better tolerated than monotherapy.
CT Check Tags: Human; Male
Adult
Aged
*Colestipol: TU, therapeutic use
Drug Therapy, Combination
***Hypercholesterolemia: DT, drug therapy**
***Hyperlipidemia: DT, drug therapy**
Lipids: BL, blood
Lipoproteins: BL, blood
***Lovastatin: TU, therapeutic use**
Middle Age
RN 50925-79-6 (Colestipol); **75330-75-5 (Lovastatin)**
CN 0 (Lipids); 0 (Lipoproteins)

L173 ANSWER 6 OF 63 MEDLINE
AN 94265237 MEDLINE
DN 94265237 PubMed ID: 8205598
TI Therapeutic use of **lovastatin** in the treatment of **hypercholesterolemia**.

AU Illingworth D R
CS Department of Medicine, Oregon Health Sciences University, Portland.
NC HL28399 (NHLBI)
P30DK40566 (NIDDK)
RR334 (NCRR)
SO CLINICAL THERAPEUTICS, **(1994 Jan-Feb)** 16 (1) 2-26; discussion 1.
Ref: 66
Journal code: CPE; 7706726. ISSN: 0149-2918.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199407
ED Entered STN: 19940721
Last Updated on STN: 19940721
Entered Medline: 19940708
AB The present review discusses the mechanism of action, efficacy, safety profile, and potential uses of **lovastatin** in patients with **hypercholesterolemia**. Data on the efficacy of **lovastatin** are evaluated in different patient populations; also, the efficacy of this agent in the long-term treatment of patients followed by the author is presented. No new safety concerns have emerged during long-term treatment of selected patients with **lovastatin**, and, in compliant patients, hypolipidemic effects are maintained during continuous treatment with therapy that exceeds 5 years. On the basis of available data, **lovastatin** should be regarded as one of the drugs of first choice in the treatment of adult patients with **hypercholesterolemia** and increased plasma concentrations of low-density lipoproteins.
CT Check Tags: Human; Support, U.S. Gov't, P.H.S.
Drug Therapy, Combination
Hydroxymethylglutaryl CoA Reductases: AI, antagonists & inhibitors
***Hypercholesterolemia: DT, drug therapy**
Hypercholesterolemia: ME, metabolism
Hyperlipidemia: DT, drug therapy
Hyperlipidemia: ME, metabolism
Lipoproteins: ME, metabolism
Lipoproteins, LDL Cholesterol: BL, blood
Lovastatin: AE, adverse effects
Lovastatin: CH, chemistry
Lovastatin: ME, metabolism
***Lovastatin: TU, therapeutic use**
Triglycerides: BL, blood
RN **75330-75-5 (Lovastatin)**
CN 0 (Lipoproteins); 0 (Lipoproteins, LDL **Cholesterol**); 0 (Triglycerides); EC 1.1.1.88 (Hydroxymethylglutaryl CoA Reductases)

L173 ANSWER 7 OF 63 MEDLINE
AN 94066432 MEDLINE
DN 94066432 PubMed ID: 7504129
TI Long-term treatment (2 years) with the HMG CoA reductase inhibitors **lovastatin** or pravastatin in combination with **cholestyramine** in patients with severe primary **hypercholesterolemia**.
AU Jacob B G; Richter W O; Schwandt P
CS Department of Medicine II, University of Munich, Germany.
SO JOURNAL OF CARDIOVASCULAR PHARMACOLOGY, **(1993 Sep)** 22 (3) 396-400.
Journal code: K78; 7902492. ISSN: 0160-2446.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199401
ED Entered STN: 19940201

Last Updated on STN: 19960129
Entered Medline: 19940104

AB The effects of the two HMG CoA reductase inhibitors **lovastatin** and pravastatin in combination with 12-16 g **cholestyramine** on serum lipids were studied in 18 patients with severe primary **hypercholesterolemia**. Combined therapy of **cholestyramine** with **lovastatin** (80 mg daily) decreased low-density-lipoprotein (LDL) **cholesterol** by 44% (baseline 7.65 +/- 0.51 mM) and increased high-density-lipoprotein (HDL) **cholesterol** by 20% (baseline 1.22 +/- 0.12 mM) in 9 patients after 2 years. In 9 other patients with comparable baseline lipid values, **cholestyramine** plus pravastatin (40 mg daily) reduced LDL **cholesterol** to a comparable extent after 2 years (-43%, baseline 7.71 +/- 0.44 mM) and increased HDL **cholesterol** by 18% (baseline 1.06 +/- 0.11 mM). The combination with **lovastatin** led to a significant reduction in triglycerides level by 25% (baseline 1.63 +/- 0.24 mM), whereas the combination with pravastatin did not change triglycerides level (baseline 1.39 +/- 0.15 mM). Both drug regimens were well tolerated without serious side effects. The effects of both HMG CoA reductase inhibitors after 2 years were comparable to those after short-term intake and after 1-year therapy without loss of efficacy.

CT Check Tags: Female; Human; Male
Adult
Aged
Cholestyramine: AD, administration & dosage
***Cholestyramine: TU, therapeutic use**
Drug Therapy, Combination
***Hypercholesterolemia: DT, drug therapy**
Lipoproteins, HDL Cholesterol: BL, blood
Lipoproteins, LDL Cholesterol: BL, blood
Lovastatin: AD, administration & dosage
***Lovastatin: TU, therapeutic use**
Middle Age
Pravastatin: AD, administration & dosage
***Pravastatin: TU, therapeutic use**
Triglycerides: BL, blood

RN **11041-12-6 (Cholestyramine)**; **75330-75-5 (Lovastatin)**; 81093-37-0 (Pravastatin)

CN 0 (Lipoproteins, HDL **Cholesterol**); 0 (Lipoproteins, LDL **Cholesterol**); 0 (Triglycerides)

L173 ANSWER 8 OF 63 MEDLINE
AN 94030808 MEDLINE
DN 94030808 PubMed ID: 8217032
TI Effect and tolerability of combining **lovastatin** with nifedipine or lisinopril.
AU Os I; Bratland B; Dahlof B; Gisholt K; Syvertsen J O; Tretli S
CS Department of Nephrology, Ulleval University Hospital, Oslo, Norway.
SO AMERICAN JOURNAL OF HYPERTENSION, **(1993 Aug)** 6 (8) 688-92.
Journal code: AJI; 8803676. ISSN: 0895-7061.
CY United States
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LA English
FS Priority Journals
EM 199312
ED Entered STN: 19940117
Last Updated on STN: 19940117
Entered Medline: 19931203

AB Single cardiovascular risk factor intervention is probably not sufficient to prevent atherosclerosis progression. There is a lack of data on concomitant use of **hypocholesterolemic** agents and antihypertensive drugs with respect to possible interactions and adverse experiences. We studied 293 patients (below 65 years of age) under treatment with either lisinopril (n = 144) or nifedipine (n = 149) for

mild to moderate hypertension for 10 weeks, and with serum **cholesterol** above 6.5 mmol/L, who were randomized to either **lovastatin** 20 mg every day or placebo in a double-blind, double-dummy design for 6 weeks. **Lovastatin** effectively lowered **cholesterol** by 16% and 15% in the lisinopril and nifedipine group respectively (P < .01 compared to placebo for both groups) without any negative impact on the antihypertensive efficacy of either lisinopril or nifedipine. The drugs in combination were well tolerated and did not affect the well-being of the patients, and did not cause any more adverse effects than the antihypertensive agents alone. Liver enzymes increased slightly during **lovastatin** therapy, while no case of myopathy was reported. Combined therapy with **lovastatin** and antihypertensive therapy can be safely undertaken.

CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't
Double-Blind Method
Drug Interactions
Drug Therapy, Combination
***Hypercholesterolemia: DT, drug therapy**
*Hypertension: DT, drug therapy
Lisinopril: AE, adverse effects
*Lisinopril: TU, therapeutic use
Lovastatin: AE, adverse effects
***Lovastatin: TU, therapeutic use**
Middle Age
Nifedipine: AE, adverse effects
*Nifedipine: TU, therapeutic use
Quality of Life
Risk Factors

RN 21829-25-4 (Nifedipine); **75330-75-5 (Lovastatin)**; 83915-83-7 (Lisinopril)

L173 ANSWER 9 OF 63 MEDLINE
AN 94023770 MEDLINE
DN 94023770 PubMed ID: 8210967
TI Effectiveness of low-dose **lovastatin** combined with low-dose colestipol in moderate to severe primary **hypercholesterolaemia**.
AU Tonstad S; Ose L; Gorbitz C; Harrison E M; de Koning Gans H J
CS Department of Medicine A, Rikshospitalet, Oslo, Norway.
SO SCANDINAVIAN JOURNAL OF CLINICAL AND LABORATORY INVESTIGATION, **(1993 Aug)** 53 (5) 457-63.
Journal code: UCP; 0404375. ISSN: 0036-5513.
CY ENGLAND: United Kingdom
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LA English
FS Priority Journals
EM 199311
ED Entered STN: 19940117
Last Updated on STN: 19950206
Entered Medline: 19931105
AB The effect of the combination of low-dose **lovastatin** and low-dose colestipol was studied among 57 subjects with moderate to severe primary **hypercholesterolaemia** (total **cholesterol** > or = 7.0 mmol l-1). Following an 8-week dietary phase, participants were randomized to treatment with 20 mg of **lovastatin** combined with 5 g or with 10 g of colestipol, or to matching placebo. Baseline total **cholesterol** was 7.7 +/- 0.9 mmol l-1 after dietary stabilization. Total **cholesterol** levels were reduced to 5.6 +/- 0.7 mmol l-1 and 5.8 +/- 0.7 mmol l-1 after 4 and 8 weeks of treatment in the **lovastatin** 5 g-1 colestipol group, and 74% of the subjects achieved the goal of low density lipoprotein (LDL) **cholesterol** levels of > or = 4.0 mmol l-1. Among the **lovastatin** 10 g-1 colestipol group, total **cholesterol** was reduced to 5.4 +/- 0.5 mmol l-1 and 5.5 +/- 0.9 mmol l-1 following 4 and 8 weeks, and 80% of subjects achieved the LDL **cholesterol** goal. No change was seen

in the placebo group. Thus, low-dose combination therapy with **lovastatin** and colestipol, in conjunction with dietary treatment, is effective in moderate to severe primary **hypercholesterolaemia**, and is well tolerated.

CT Check Tags: Female; Human; Male
Adult
Aged
Cholesterol: BL, blood
*Colestipol: AD, administration & dosage
Colestipol: AE, adverse effects
Drug Therapy, Combination
Hydroxymethylglutaryl CoA Reductases: AI, antagonists & inhibitors
***Hypercholesterolemia: DT, drug therapy**
***Lovastatin: AD, administration & dosage**
Lovastatin: AE, adverse effects
Middle Age

RN 50925-79-6 (Colestipol); **57-88-5 (Cholesterol); 75330-75-5 (Lovastatin)**

CN EC 1.1.1.88 (Hydroxymethylglutaryl CoA Reductases)

L173 ANSWER 10 OF 63 MEDLINE
AN 93326083 MEDLINE
DN 93326083 PubMed ID: 8333817
TI Combination drug therapy for **hypercholesterolemia**. The trade-off between cost and simplicity.
AU Heudebert G R; Van Ruiswyk J; Hiatt J; Schectman G
CS Department of Medicine, Medical College of Wisconsin, Zablocki Veterans Affairs Medical Center, Milwaukee.
SO ARCHIVES OF INTERNAL MEDICINE, **(1993 Aug 9)** 153 (15) 1828-37.
Journal code: 7FS; 0372440. ISSN: 0003-9926.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199308
ED Entered STN: 19930826
Last Updated on STN: 19930826
Entered Medline: 19930819

AB BACKGROUND: The National **Cholesterol** Education Program recommends achievement of a defined target level of low-density lipoprotein **cholesterol** (LDL-C) for the treatment of **hypercholesterolemia**. They endorse the use of niacin and/or sequestrants as the first line of therapy to achieve such target LDL-C level. This recommendation has not been compared with the use of **lovastatin** as initial therapy if multidrug regimens are required to achieve goal LDL-C. METHODS: Prospectively collected data on tolerance and effectiveness for niacin, sequestrants, and **lovastatin** were obtained from a lipid clinic at a large midwestern Veterans Affairs medical center. We used a decision tree to compare the complexity and cost of three sequential drug algorithms used for the following initial LDL-C levels: 4.14, 4.91, 5.69, and 6.47 mmol/L (160, 190, 220, and 250 mg/dL). Algorithm 1 was niacin followed by a sequestrant and then **lovastatin**; algorithm 2, a sequestrant followed by niacin and then **lovastatin**; and algorithm 3, **lovastatin** followed by niacin and a sequestrant. Drug and laboratory costs were obtained from the pharmacy and pathology services at the same institution. Sensitivity analyses were performed on the tolerance and effectiveness of each drug as well as drug and laboratory cost estimates. RESULTS: The probability of achieving target LDL-C level (3.36 mmol/L [130 mg/dL]) decreased as initial LDL-C level increased. As a rule, algorithm 3 required fewer drugs in combination to achieve the target level for all initial LDL-C levels modeled. In addition, the use of **lovastatin** was high across all algorithms at all initial LDL-C levels modeled. Algorithm 1 was less expensive than algorithm 2 or 3 at a low initial LDL-C level (4.14 mmol/L [160 mg/dL]), with an average cost of $375 vs $454 vs $585, respectively. At all other initial LDL-C levels (4.91, 5.69, and 6.47 mmol/L [190, 220,

and 250 mg/dL]), algorithm 2 was slightly less expensive than algorithm 1. Algorithm 3 became relatively less expensive as initial LDL-C level increased: 56% more expensive than algorithm 1 at an initial LDL-C level of 4.14 mmol/L (160 mg/dL) as compared with 7% more expensive than algorithm 1 at an initial LDL-C level of 6.47 mmol/L (250 mg/dL). CONCLUSIONS: Fulfillment of the target LDL-C approach recommended by the National **Cholesterol** Education Program often requires the use of multiple drugs. When **lovastatin** is used initially, the regimen becomes simpler, albeit more expensive. At initial LDL-C levels of 4.91 mmol/L (190 mg/dL) or higher, this difference in cost becomes progressively smaller (7% at 6.47 mmol/L [250 mg/dL]), making algorithm 3 the better alternative; at low initial LDL-C levels (4.14 mmol/L [160 mg/dL]), a niacin-first regimen is reasonably simple and substantially less expensive. At moderate and severe initial LDL-C levels (4.91 and 5.69 mmol/L [190 and 220 mg/dL]), the **lovastatin**-first regimen may be advantageous.

CT Check Tags: Female; Human; Male; Support, U.S. Gov't, Non-P.H.S.
Aged
Algorithms
***Anticholesteremic Agents: AD, administration & dosage**
Anticholesteremic Agents: EC, economics
Decision Trees
Drug Costs
Drug Therapy, Combination
Hospitals, Veterans
***Hypercholesterolemia: DT, drug therapy**
Hypercholesterolemia: EC, economics
Lovastatin: TU, therapeutic use
Middle Age
Midwestern United States
Niacin: TU, therapeutic use
Probability
Prospective Studies
Treatment Outcome

RN 59-67-6 (Niacin); **75330-75-5 (Lovastatin)**
CN 0 (**Anticholesteremic** Agents)

L173 ANSWER 11 OF 63 MEDLINE
AN 93321450 MEDLINE
DN 93321450 PubMed ID: 8330475
TI Evidence of combined therapy of dyslipoproteinemia by HMG-CoA reductase inhibitors and "essential" phospholipids.
AU Gurevich V S; Bondarenko B B; Mikhailova I A; Kasennova N I; Popov YuG; Astashkina; Le Van Thach T D
CS Cardiology Institute, S. Petersburg, Russia.
SO CLINICA TERAPEUTICA, **(1993 Apr)** 142 (4) 329-34.
Journal code: DKN; 0372604. ISSN: 0009-9074.
CY Italy
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199308
ED Entered STN: 19930826
Last Updated on STN: 19930826
Entered Medline: 19930819
AB Platelets are involved in the initiation of atheromas and arterial thrombosis and thus may play a cardinal role in the pathogenesis of myocardial and cerebral infarction. In 18 patients with coronary artery disease and **hypercholesterolemia** resistant to low-lipid diet a 12 week treatment with **lovastatin** (HMG-CoA reductase inhibitor) leads to the reduction of total **cholesterol**, LDL-**cholesterol** and triglycerides but also to a marked increase of platelet activity. **Lovastatin** is an inactive lacton prodrug which must be enzymatically or chemically transformed to the active form. In in-vitro experiments, it was discovered that both chemically hydrolysed **lovastatin** and plasma containing **lovastatin** metabolites

stimulate induced platelet aggregation in whole blood samples. "Essential" phospholipids (Lipostabil) added to the blood samples in concentrations according to those which are used clinically prevent this stimulation. This corresponds to data obtained earlier from Lipostabil-treated ischemic heart disease patients. Besides a lipid-lowering effect Lipostabil showed a 50% reduction of spontaneous aggregates in plasma, an increase of the susceptibility threshold to aggregation inducers and a decrease of the platelet aggregation amplitude in whole blood samples. Therefore, it would be promising to combine the therapy by **lovastatin** with "essential" phospholipids possessing a remarkable improving effect on the platelet function based on a molecular action independent of their moderate lipid-reducing action.

CT Check Tags: Human; Male
Adult
Cholesterol: BL, blood
Coronary Disease: BL, blood
*Coronary Disease: DT, drug therapy
Drug Therapy, Combination
Hypercholesterolemia: BL, blood
***Hypercholesterolemia: DT, drug therapy**
Lipoproteins, LDL: BL, blood
***Lovastatin: TU, therapeutic use**
Phosphatidylcholines: PD, pharmacology
*Phosphatidylcholines: TU, therapeutic use
Platelet Aggregation: DE, drug effects

RN 11096-62-1 (lipostabil); **57-88-5 (Cholesterol)**; **75330-75-5 (Lovastatin)**

CN 0 (Lipoproteins, LDL); 0 (Phosphatidylcholines)

L173 ANSWER 12 OF 63 MEDLINE

AN 93299805 MEDLINE

DN 93299805 PubMed ID: 8519043

TI Treatment of severe, resistant familial combined hyperlipidemia with a bezafibrate-**lovastatin** combination.

AU Yeshurun D; Abukarshin R; Elias N; Lanir A; Naschitz J E

CS Department of Medicine A, B'nai Zion Medical Center, Technion, Haifa, Israel.

SO CLINICAL THERAPEUTICS, **(1993 Mar-Apr)** 15 (2) 355-63.
Journal code: CPE; 7706726. ISSN: 0149-2918.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199307

ED Entered STN: 19930813
Last Updated on STN: 19930813
Entered Medline: 19930726

AB Familial combined hyperlipidemia (FCHL) is a common lipid disorder characterized by high levels of **cholesterol**, triglycerides, or both. The basic metabolic abnormality is overproduction of apolipoprotein B-100. High atherogenicity has been attributed to all forms of FCHL. We evaluated combined bezafibrate-**lovastatin** therapy in 10 patients (9 men and 1 woman) with FCHL and markedly high **cholesterol** and triglyceride levels who were at high risk of coronary artery disease and who had not responded to diet and bezafibrate treatment alone. Eight patients had coronary artery disease, 6 had hypertension, and 3 had noninsulin-dependent diabetes mellitus. **Lovastatin** 20 mg/day was added to the bezafibrate 600 mg/day regimen for 6 weeks; the **lovastatin** dosage was then doubled to 40 mg/day for an additional 6 weeks. The addition of 20 mg of **lovastatin** resulted in decreases of 15%, 20%, and 13% in total **cholesterol**, low-density lipoprotein (LDL) **cholesterol**, and triglyceride levels, respectively. Increasing the dose of **lovastatin** to 40 mg resulted in further moderate decreases of 4%, 3%, and 8% in total **cholesterol**, LDL **cholesterol**, and triglycerides, respectively, compared with the 20 mg/day dosage. Although previous

reports have emphasized the potential side effects of combination treatment with **lovastatin** and fibric acid derivatives, our patients tolerated the regimen well, with no significant subjective complaints or laboratory abnormalities. The bezafibrate-**lovastatin** combination is a possible therapeutic option for severe, resistant FCHL, but close medical supervision is needed because of potential side effects.

CT Check Tags: Female; Human; Male
Adult
Bezafibrate: AD, administration & dosage
Bezafibrate: AE, adverse effects
***Bezafibrate: TU, therapeutic use**
Cholesterol: BL, blood
Drug Resistance
Drug Therapy, Combination
***Hyperlipidemia, Familial Combined: DT, drug therapy**
Lipoproteins, HDL: BL, blood
Lipoproteins, LDL Cholesterol: BL, blood
Lipoproteins, VLDL: BL, blood
Lovastatin: AD, administration & dosage
Lovastatin: AE, adverse effects
***Lovastatin: TU, therapeutic use**
Middle Age
Triglycerides: BL, blood

RN 41859-67-0 (Bezafibrate); **57-88-5 (Cholesterol)**; **75330-75-5 (Lovastatin)**

CN 0 (Lipoproteins, HDL); 0 (Lipoproteins, LDL **Cholesterol**); 0 (Lipoproteins, VLDL); 0 (Triglycerides)

L173 ANSWER 13 OF 63 MEDLINE
AN 93110603 MEDLINE
DN 93110603 PubMed ID: 1471127
TI [**Lovastatin** in primary **hypercholesterolemia**. A Norwegian multicenter study].
Lovastatin ved primaer hyperkolesterolemi. En norsk multisenterstudie.
AU Ose L
CS Lipidklinikken, Rikshospitalet, Oslo.
SO TIDSSKRIFT FOR DEN NORSKE LAEGEFORENING, **(1992 Nov 30)** 112 (29) 3665-9.
Journal code: VRV; 0413423. ISSN: 0029-2001.
CY Norway
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
LA Norwegian
FS Priority Journals
EM 199301
ED Entered STN: 19930212
Last Updated on STN: 19930212
Entered Medline: 19930127
AB 266 patients with primary **hypercholesterolaemia** were followed for 48 weeks at 27 different centres to evaluate the safety, tolerability and effect on plasma lipids of **lovastatin** ranging from 20 to 80 mg/day. Mean change from baseline after 12 weeks of treatment with **lovastatin** was -34% (CI:33-35) for total **cholesterol**, -42% (CI:40-43) for LDL-**cholesterol**, +14% (CI:12-17) for HDL-**cholesterol** and -14% (CI:10-18) for triglycerides. Combination therapy with **cholestyramine** (8-24 g/day) was optional, and was started in 89 patients from week 13. At week 48 only 25% of all patients had obtained the second objective of the study: a total **cholesterol** value below 5.2 mmol/l. At the same time 60% of all patients had a total **cholesterol** below 6.2 mmol/l. Four patients dropped out of the study owing to adverse clinical experience. Only three of these events were probably related to **lovastatin**. Six patients were withdrawn because of adverse laboratory experiences. One patient showed clinical signs of myositis and increase of CK. In severe

primary **hypercholesterolaemia** combination therapy with **lovastatin** and a resin such as **cholestyramine** is required to obtain total **cholesterol** values below 5.2 mmol/l.

CT Check Tags: Female; Human; Male
Adult
Aged
Cholesterol: BL, blood
***Cholestyramine: AD, administration & dosage**
Cholestyramine: AE, adverse effects
Drug Evaluation
Drug Therapy, Combination
Hypercholesterolemia: BL, blood
***Hypercholesterolemia: DT, drug therapy**
***Lovastatin: AD, administration & dosage**
Lovastatin: AE, adverse effects
Middle Age
Triglycerides: BL, blood

RN **11041-12-6 (Cholestyramine); 57-88-5 (Cholesterol); 75330-75-5 (Lovastatin)**

CN 0 (Triglycerides)

L173 ANSWER 14 OF 63 MEDLINE

AN 93096336 MEDLINE

DN 93096336 PubMed ID: 1461539

TI [Clinical evaluation of a selective inhibitor of **cholesterol** synthesis: pravastatin].
Valutazione clinica di un inibitore selettivo della sintesi del colesterolo: la pravastatina.

AU Alessandri C; Peverini F

CS Universita degli Studi di Roma La Sapienza, Roma.

SO MINERVA MEDICA, **(1992 Nov)** 83 (11) 677-93. Ref: 98
Journal code: N6M; 0400732. ISSN: 0026-4806.

CY Italy

DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)

LA Italian

FS Priority Journals

EM 199301

ED Entered STN: 19930129
Last Updated on STN: 19980206
Entered Medline: 19930114

AB The recent introduction in clinical practice of a new class of drugs able to reduce the endogenous synthesis of **cholesterol** has undoubtedly made a noteworthy contribution to the treatment of **hypercholesterolaemia** which, as is well known, is one of the greatest risk factors in the natural history of atherosclerotic disease and of its cardiovascular complications. A last generation drug belonging to this family is pravastatin which differs from the other substances inhibiting the activity of the key enzyme of **cholesterol** metabolism, HMGCaA reductase, because of certain features of the molecule, such as hydrophilia and the fact it is already pharmacologically active at the moment of oral administration. Pravastatin, which is probably a special category of HMGCoA reductase inhibitor, has shown, in numerous experimental studies and controlled clinical trials, a notable effectiveness in reducing in a highly selective fashion the synthesis of **cholesterol** in the liver cells and consequently the number of **cholesterol**-rich lipoproteins in the systemic circulation, without also determining significant biologically negative side-effects.

CT Check Tags: Animal; Comparative Study; Female; Human; Male
Adult
Anticholesteremic Agents: AD, administration & dosage
Anticholesteremic Agents: TU, therapeutic use
Cholesterol: BI, biosynthesis
Cholestyramine: TU, therapeutic use
Clinical Trials

Drug Therapy, Combination
Guinea Pigs
Hydroxymethylglutaryl CoA Reductases: AI, antagonists & inhibitors
***Hypercholesterolemia: DT, drug therapy**
Hypercholesterolemia: ET, etiology
Lovastatin: AA, analogs & derivatives
Lovastatin: TU, therapeutic use
Pravastatin: AD, administration & dosage
Pravastatin: AE, adverse effects
***Pravastatin: TU, therapeutic use**
Rats
Risk Factors
Simvastatin
Time Factors
RN **11041-12-6 (Cholestyramine)**; **57-88-5 (Cholesterol)**; **75330-75-5 (Lovastatin)**; 79902-63-9 (Simvastatin); 81093-37-0 (Pravastatin)
CN 0 (**Anticholesteremic** Agents); EC 1.1.1.88 (Hydroxymethylglutaryl CoA Reductases)

L173 ANSWER 15 OF 63 MEDLINE
AN 93031643 MEDLINE
DN 93031643 PubMed ID: 1412289
TI [Familial **hypercholesterolemia**--intensive diet therapy combined with drug therapy].
Familiaer hyperkolesterolemi--intensiv kostbehandling i kombinasjon med medikamentell behandling.
AU Stugaard M; Wiig I; Lund H; Ose L; Norseth J
CS Medisinsk avdeling A, Rikshospitalet, Oslo.
SO TIDSSKRIFT FOR DEN NORSKE LAEGEFORENING, **(1992 Aug 30)** 112 (20) 2642-6.
Journal code: VRV; 0413423. ISSN: 0029-2001.
CY Norway
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LA Norwegian
FS Priority Journals
EM 199211
ED Entered STN: 19930122
Last Updated on STN: 19930122
Entered Medline: 19921120
AB The aim of the investigation was twofold: to study the effect of **lovastatin**, a potent inhibitor of 3-hydroxy-3-methylglutaryl coenzyme A reductase, alone and in combination with other lipid lowering drugs in an open 48 week single centre study, and to study if lipid lowering drugs influence adherence to diet in adult patients with familial **hypercholesterolemia**. **Lovastatin** monotherapy (80 mg daily) for 12 weeks reduced serum **cholesterol**, LDL-**cholesterol** and triglycerides levels by 36%, 44% and 24% respectively. HDL-**cholesterol** level was increased by 12%. The addition of 16 g **cholestyramine** daily further increased the reduction of total **cholesterol** and LDL-**cholesterol** levels by 17% and 24% respectively. Addition of 1 g probucol daily decreased total **cholesterol**, LDL-**cholesterol** and HDL-**cholesterol** levels by 9%, 5% and 27% respectively. Addition of omega-3-fatty acids (3.6 g daily) reduced total **cholesterol**, LDL-**cholesterol** and triglycerides levels by 10%, 12% and 20% respectively. Administration of potent lipid lowering agents did not influence adherence to a diet with a mean daily fat energy of 21% (CI: 20-22), **cholesterol** of 177 mg (CI: 157-196) and P/S ratio of 0.75 (CI: 0.66-0.84). A significant increase in liver enzymes was recorded in only one patient. One patient was withdrawn from the study because of myositis.
CT Check Tags: Human
Adolescence
Adult

Aged
Antilipemic Agents: AE, adverse effects
*Antilipemic Agents: TU, therapeutic use
Cholestyramine: AE, adverse effects
Cholestyramine: TU, therapeutic use
Drug Evaluation
Drug Therapy, Combination
Hypercholesterolemia, Familial: BL, blood
Hypercholesterolemia, Familial: DH, diet therapy
***Hypercholesterolemia, Familial: DT, drug therapy**
Lovastatin: AE, adverse effects
***Lovastatin: TU, therapeutic use**
Middle Age
RN **11041-12-6 (Cholestyramine); 75330-75-5 (Lovastatin)**
CN 0 (Antilipemic Agents)

L173 ANSWER 16 OF 63 MEDLINE
AN 93024015 MEDLINE
DN 93024015 PubMed ID: 1406395
TI Successful management of primary **hypercholesterolaemia** with simvastatin and low-dose colestipol.
AU Simons L A; Simons J; Parfitt A
CS University of New South Wales, School of Medicine, Darlinghurst.
SO MEDICAL JOURNAL OF AUSTRALIA, **(1992 Oct 5)** 157 (7) 455-9.
Journal code: M26; 0400714. ISSN: 0025-729X.
CY Australia
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LA English
FS Priority Journals
EM 199210
ED Entered STN: 19930122
Last Updated on STN: 19980206
Entered Medline: 19921028
AB OBJECTIVE: To examine whether a small dose of bile acid sequestrant used in combination with a hydroxymethylglutaryl coenzyme A reductase inhibitor is more effective in reducing serum and low-density lipoprotein (LDL) **cholesterol** levels than inhibitor used alone. DESIGN: A randomised, double-blind study. SETTING: Subjects receiving tertiary care at a hospital lipid clinic. PATIENTS: Subjects with severe primary **hypercholesterolaemia** (types IIa and IIb), already stabilised on a **cholesterol**-lowering diet, with serum **cholesterol** levels of 7.0 mmol/L or more and triglyceride levels of 6.0 mmol/L or less. Sixty-four subjects were randomly assigned to the treatment groups; three withdrew before any outcome observations; 61 completed the trial and their results were analysed. INTERVENTIONS: Subjects were randomly assigned to receive either colestipol placebo or colestipol 5 g or 10 g each morning in fixed dosage for 18 weeks. They simultaneously received incremental doses of simvastatin: placebo for six weeks, then 20 mg/night for six weeks, then 40 mg/night for a final six weeks. MAIN OUTCOME MEASURES: Lipids, lipoproteins, and haematological and biochemical safety parameters were measured at the end of each treatment period. Adverse events were monitored. RESULTS: Respective maximum reductions (95% confidence intervals) in serum **cholesterol**, LDL **cholesterol** and apolipoprotein B (apo-B) values in subjects taking combination therapy were 41% (38%-45%), 50% (46%-53%) and 43% (39%-46%), compared with lesser reductions of 32% (26%-37%), 38% (31%-45%) and 37% (32%-41%) in those taking simvastatin monotherapy. The percentage changes in LDL **cholesterol** with combination therapy were independent of baseline **cholesterol** level or lipid phenotype. Combination therapy reduced serum triglyceride levels by up to 24% (15%-32%) and increased high-density lipoprotein (HDL) **cholesterol** levels by up to 9% (3%-15%). Three subjects withdrew within a few weeks because of severe gastrointestinal side effects related to colestipol; 19 experienced milder gastrointestinal side effects, 15 were taking combination therapy.

CONCLUSIONS: A combination of low-dose colestipol and simvastatin was found to be more effective in reducing serum and LDL **cholesterol** than simvastatin used alone. Such combination therapy offers the possibility of improved **cholesterol** lowering without the need for full dosage of either drug.

CT Check Tags: Human; Support, Non-U.S. Gov't
***Anticholesteremic Agents: AD, administration & dosage**
Anticholesteremic Agents: TU, therapeutic use
Apolipoproteins B: BL, blood
Cholesterol: BL, blood
*Colestipol: AD, administration & dosage
Colestipol: TU, therapeutic use
Double-Blind Method
Drug Therapy, Combination
Hypercholesterolemia: BL, blood
***Hypercholesterolemia: DT, drug therapy**
Lipoproteins, HDL: BL, blood
Lipoproteins, LDL Cholesterol: BL, blood
Lovastatin: AD, administration & dosage
***Lovastatin: AA, analogs & derivatives**
Lovastatin: TU, therapeutic use
Simvastatin
Treatment Outcome
Triglycerides: BL, blood

RN 50925-79-6 (Colestipol); **57-88-5 (Cholesterol)**; **75330-75-5 (Lovastatin)**; 79902-63-9 (Simvastatin)

CN 0 (**Anticholesteremic** Agents); 0 (Apolipoproteins B); 0 (Lipoproteins, HDL); 0 (Lipoproteins, LDL **Cholesterol**); 0 (Triglycerides)

L173 ANSWER 17 OF 63 MEDLINE
AN 93005427 MEDLINE
DN 93005427 PubMed ID: 1392453
TI Long-term effect of **lovastatin** alone and in combination with **cholestyramine** on lipoprotein (a) level in familial **hypercholesterolemic** subjects.
AU Leren T P; Hjermann I; Foss O P; Leren P; Berg K
CS Department of Medical Genetics, Ullevaal Hospital, Oslo.
SO CLINICAL INVESTIGATOR, **(1992 Aug)** 70 (8) 711-8.
Journal code: BHE; 9207154. ISSN: 0941-0198.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199211
ED Entered STN: 19930122
Last Updated on STN: 19930122
Entered Medline: 19921117
AB We have determined the effect of **lovastatin** alone or in combination with **cholestyramine** on lipoprotein (a) [Lp(a)] levels in 59 heterozygotes for familial **hypercholesterolemia** (FH) treated for 33.8 (+/- 6.1) months. The median pretrial Lp(a) value was 10.2 mg/100 ml, which is twice the median value in healthy people examined at the Institute of Medical Genetics, University of Oslo. The median Lp(a) level was insignificantly reduced by 10.3% during the first 20 weeks when the subjects were on a standardized medication of increasing doses of **lovastatin** and **cholestyramine**. The first 20 weeks were followed by usual care treatment period, and a further decrease in Lp(a) level to 16.2% (P = 0.0012) was observed at the end of the study. Comparison between the 20 subjects on **lovastatin** monotherapy and the 31 subjects on the combined therapy of **lovastatin** and **cholestyramine**, revealed that the subjects on monotherapy had a median reduction of 20.1%, and the subjects on the combined therapy had a reduction of 15.4%. Thus, it appears that the reduction in Lp(a) level could be ascribed to **lovastatin** alone.
CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't

Adolescence
Adult
Aged
Apolipoproteins: BL, blood
***Cholestyramine: AD, administration & dosage**
Cholestyramine: AE, adverse effects
Drug Therapy, Combination
Follow-Up Studies
Heterozygote
Hypercholesterolemia, Familial: BL, blood
***Hypercholesterolemia, Familial: DT, drug therapy**
Lipids: BL, blood
*Lipoprotein(a): BL, blood
Lipoproteins: BL, blood
***Lovastatin: AD, administration & dosage**
Lovastatin: AE, adverse effects
Middle Age
Time Factors
RN **11041-12-6 (Cholestyramine); 75330-75-5 (Lovastatin)**
CN 0 (Apolipoproteins); 0 (Lipids); 0 (Lipoprotein(a)); 0 (Lipoproteins)

L173 ANSWER 18 OF 63 MEDLINE
AN 92387196 MEDLINE
DN 92387196 PubMed ID: 1516599
TI Short- and long-term effects of **lovastatin** and pravastatin alone and in combination with **cholestyramine** on serum lipids, lipoproteins and apolipoproteins in primary **hypercholesterolaemia**.
AU Jacob B G; Mohrle W; Richter W O; Schwandt P
CS Department of Medicine II, University of Munich, FRG.
SO EUROPEAN JOURNAL OF CLINICAL PHARMACOLOGY, **(1992)** 42 (4) 353-8.
Journal code: EN4; 1256165. ISSN: 0031-6970.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199210
ED Entered STN: 19921023
Last Updated on STN: 19921023
Entered Medline: 19921006
AB The effects of the HMG CoA reductase inhibitors **lovastatin** and pravastatin on serum lipids, lipoproteins and apolipoproteins have been studied in 35 patients with primary **hypercholesterolaemia**. LDL **cholesterol** was lowered to the same extent by both agents compared on a mg basis of each drug per day. HDL **cholesterol** was increased by **lovastatin** but not by pravastatin. The reduction in serum triglycerides, VLDL triglycerides and VLDL **cholesterol** was more pronounced after **lovastatin** than pravastatin. After 1 year the effect of combined treatment with 40 mg pravastatin and 8 g **cholestyramine** on the reduction in LDL **cholesterol** (-39%) in 13 patients was comparable to that of 80 mg **lovastatin** plus 8 g **cholestyramine** (-40%) in 12 patients with identical baseline values. Differences were also found in the effects of the combination therapy with the two drugs on HDL **cholesterol**, serum triglycerides, VLDL triglycerides, VLDL **cholesterol**, and apolipoproteins.
CT Check Tags: Comparative Study; Female; Human; Male
Adolescence
Adult
Aged
Aged, 80 and over
*Apolipoproteins: BL, blood
Apolipoproteins: DE, drug effects
Cholesterol: BL, blood
***Cholestyramine: PD, pharmacology**
Drug Therapy, Combination

Hypercholesterolemia: BL, blood
***Hypercholesterolemia: DT, drug therapy**
*Lipids: BL, blood
*Lipoproteins: BL, blood
Lipoproteins: DE, drug effects
Lipoproteins, HDL Cholesterol: BL, blood
Lipoproteins, LDL Cholesterol: BL, blood
Lipoproteins, VLDL Cholesterol: BL, blood
***Lovastatin: PD, pharmacology**
Middle Age
***Pravastatin: PD, pharmacology**
Time Factors
Triglycerides: BL, blood
RN **11041-12-6 (Cholestyramine); 57-88-5 (Cholesterol); 75330-75-5 (Lovastatin);** 81093-37-0 (Pravastatin).
CN 0 (Apolipoproteins); 0 (Lipids); 0 (Lipoproteins); 0 (Lipoproteins, HDL **Cholesterol**); 0 (Lipoproteins, LDL **Cholesterol**); 0 (Lipoproteins, VLDL **Cholesterol**); 0 (Triglycerides)

L173 ANSWER 19 OF 63 MEDLINE
AN 92312488 MEDLINE
DN 92312488 PubMed ID: 1615846
TI Gemfibrozil-**lovastatin** therapy for primary hyperlipoproteinemias.
CM Comment in: Am J Cardiol. 1993 Feb 15;71(5):497
AU Glueck C J; Oakes N; Speirs J; Tracy T; Lang J
CS Cholesterol Center, Jewish Hospital, Cincinnati, Ohio 45229.
SO AMERICAN JOURNAL OF CARDIOLOGY, **(1992 Jul 1)** 70 (1) 1-9.
Journal code: 3DQ; 0207277. ISSN: 0002-9149.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199207
ED Entered STN: 19920807
Last Updated on STN: 19920807
Entered Medline: 19920730
AB The specific aim of this retrospective, observational study was to assess safety and efficacy of long-term (21 months/patient), open-label, gemfibrozil-**lovastatin** treatment in 80 patients with primary mixed hyperlipidemia (68% of whom had atherosclerotic vascular disease). Because ideal lipid targets were not reached (low-density lipoprotein (LDL) **cholesterol** less than 130 mg/dl, high-density lipoprotein (HDL) **cholesterol** greater than 35 mg/dl, or total **cholesterol**/HDL **cholesterol** less than 4.5 mg/dl) with diet plus a single drug, gemfibrozil (1.2 g/day)-**lovastatin** (primarily 20 or 40 mg) treatment was given. Follow-up visits were scheduled with 2-drug therapy every 6 to 8 weeks, an average of 10.3 visits per patient, with 741 batteries of 6 liver function tests and 714 creatine phosphokinase levels measured. Only 1 of the 4,446 liver function tests (0.02%), a gamma glutamyl transferase, was greater than or equal to 3 times the upper normal limit. Of the 714 creatine phosphokinase levels, 9% were high; only 1 (0.1%) was greater than or equal to 3 times the upper normal limit. With 2-drug therapy, mean total **cholesterol** decreased 22% from 255 to 200 mg/dl, triglyceride levels decreased 35% from 236 to 154 mg/dl, LDL **cholesterol** decreased 26% from 176 to 131 mg/dl, and the total **cholesterol**/HDL **cholesterol** ratio decreased 24% from 7.1 to 5.4, all p less than or equal to 0.0001. Myositis, attributable to the drug combination and symptomatic enough to discontinue it, occurred in 3% of patients, and in 1% with concurrent high creatine phosphokinase (769 U/liter); no patients had rhabdomyolysis or myoglobinuria.(ABSTRACT TRUNCATED AT 250 WORDS)
CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't
Adult
Aged
Analysis of Variance

Cholesterol: BL, blood
Combined Modality Therapy
Creatine Kinase: BL, blood
Drug Therapy, Combination
Gemfibrozil: AE, adverse effects
*Gemfibrozil: TU, therapeutic use
Hyperlipoproteinemia: BL, blood
Hyperlipoproteinemia: DH, diet therapy
***Hyperlipoproteinemia: DT, drug therapy**
Liver Function Tests
Lovastatin: AE, adverse effects
***Lovastatin: TU, therapeutic use**
Middle Age
Myositis: CI, chemically induced
Retrospective Studies
Triglycerides: BL, blood
RN 25812-30-0 (Gemfibrozil); **57-88-5 (Cholesterol)**; **75330-75-5 (Lovastatin)**
CN 0 (Triglycerides); EC 2.7.3.2 (Creatine Kinase)

L173 ANSWER 20 OF 63 MEDLINE
AN 92275541 MEDLINE
DN 92275541 PubMed ID: 1592346
TI Effect of simvastatin, ursodeoxycholic acid and simvastatin plus ursodeoxycholic acid on biliary lipid secretion and cholic acid kinetics in nonfamilial **hypercholesterolemia.**
AU Mazzella G; Parini P; Festi D; Bazzoli F; Aldini R; Roda A; Tonelli D; Cipolla A; Salzetta A; Roda E
CS Cattedra di Gastroenterologia, University of Bologna, Italy.
SO HEPATOLOGY, **(1992 Jun)** 15 (6) 1072-8.
Journal code: GBZ; 8302946. ISSN: 0270-9139.
CY United States
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LA English
FS Priority Journals
EM 199206
ED Entered STN: 19920710
Last Updated on STN: 19990129
Entered Medline: 19920626
AB It has been recently shown that the newest **hypocholesterolemic** agent, simvastatin, lowers the biliary **cholesterol** saturation index and that its association with ursodeoxycholic acid renders it more effective. To determine the mechanism by which simvastatin decreases the biliary **cholesterol** saturation index, we evaluated hepatic secretion rates of **cholesterol**, bile acids and phospholipids, and cholic acid pool size, turnover and synthesis in eight hyperlipidemic patients (five women and three men, age range = 38 to 65 yr). These assessments were conducted before treatment, after 4 wk of simvastatin (40 mg/day), after 4 wk of ursodeoxycholic acid (600 mg/day) and after a further 4 wk of a combination therapy of simvastatin (40 mg/day) plus ursodeoxycholic acid (600 mg/day). The **cholesterol** saturation index was significantly reduced with simvastatin (from 1.51 +/- 0.10 to 0.94 +/- 0.05, mean +/- S.E.; p less than 0.02), with ursodeoxycholic acid (from 1.51 +/- 0.10 to 0.86 +/- 0.03, mean +/- S.E.; p less than 0.02) and with the combination of simvastatin plus ursodeoxycholic acid (from 1.51 +/- 0.01 to 0.70 +/- 0.05, p less than 0.02). The **cholesterol** saturation index during combination therapy was significantly lower (p less than 0.02) than that reached during the use of simvastatin and ursodeoxycholic acid. Both simvastatin and ursodeoxycholic acid significantly reduced the hepatic secretion rate of **cholesterol** (from 130 +/- 14 mumols/hr to 81 +/- 12 mumols/hr, p less than 0.01, and 70 +/- 9 mumols/hr, p less than 0.01) without affecting bile acid and phospholipid outputs.(ABSTRACT TRUNCATED AT 250 WORDS)
CT Check Tags: Female; Human; Male

Adult
Aged
***Anticholesteremic Agents: TU, therapeutic use**
*Bile: ME, metabolism
Cholesterol: ME, metabolism
Cholic Acid
Cholic Acids: BI, biosynthesis
*Cholic Acids: ME, metabolism
Drug Therapy, Combination
Hydroxymethylglutaryl CoA Reductases: AI, antagonists & inhibitors
***Hypercholesterolemia: DT, drug therapy**
Hypercholesterolemia: ME, metabolism
Kinetics
*Lipids: ME, metabolism
Liver: ME, metabolism
***Lovastatin: AA, analogs & derivatives**
Lovastatin: TU, therapeutic use
Middle Age
Simvastatin
*Ursodeoxycholic Acid: TU, therapeutic use
RN 128-13-2 (Ursodeoxycholic Acid); **57-88-5 (Cholesterol)**; **75330-75-5 (Lovastatin)**; 79902-63-9 (Simvastatin); 81-25-4 (Cholic Acid)
CN 0 (**Anticholesteremic** Agents); 0 (Cholic Acids); 0 (Lipids); EC 1.1.1.88 (Hydroxymethylglutaryl CoA Reductases)

L173 ANSWER 21 OF 63 MEDLINE
AN 92247097 MEDLINE
DN 92247097 PubMed ID: 1811555
TI Response to **cholesterol**-lowering drugs in familial defective apolipoprotein B-100.
AU Maher V M; Gallagher J J; Thompson G R; Myant N B
CS MRC Lipoprotein Team, Hammersmith Hospital, London, U.K.
SO ATHEROSCLEROSIS, **(1991 Nov)** 91 (1-2) 73-6.
Journal code: 95X; 0242543. ISSN: 0021-9150.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199206
ED Entered STN: 19920619
Last Updated on STN: 19980206
Entered Medline: 19920603
AB The effect of **cholestyramine** and simvastatin, given separately or in combination, on serum lipid concentrations in 11 patients with heterozygous familial defective apolipoprotein B-100 was compared with that in 11 matched patients with heterozygous familial **hypercholesterolaemia**. In both groups of patients there was a substantial fall in serum lipid levels in response to treatment. There were no significant differences between the reductions in serum total or low-density lipoprotein **cholesterol** levels in the two groups.
CT Check Tags: Comparative Study; Female; Human; Male; Support, Non-U.S. Gov't
Adult
Aged
***Anticholesteremic Agents: TU, therapeutic use**
*Apolipoproteins B: GE, genetics
Apolipoproteins E: GE, genetics
Cholesterol: BL, blood
Cholestyramine: TU, therapeutic use
Drug Therapy, Combination
Heterozygote
Hypercholesterolemia: BL, blood
***Hypercholesterolemia: DT, drug therapy**
Hypercholesterolemia: GE, genetics
Lipoproteins, LDL Cholesterol: BL, blood

Lovastatin: AA, analogs & derivatives
Lovastatin: TU, therapeutic use
Middle Age
Phenotype
Simvastatin
Triglycerides: BL, blood
RN **11041-12-6 (Cholestyramine); 57-88-5 (Cholesterol); 75330-75-5 (Lovastatin);** 79902-63-9 (Simvastatin)
CN 0 (**Anticholesteremic** Agents); 0 (Apolipoproteins B); 0 (Apolipoproteins E); 0 (Lipoproteins, LDL **Cholesterol**); 0 (Triglycerides); 0 (apolipoprotein B-100)

L173 ANSWER 22 OF 63 MEDLINE
AN 92177766 MEDLINE
DN 92177766 PubMed ID: 1724525
TI Combination therapy with **lovastatin** and guar gum versus **lovastatin** and **cholestyramine** in treatment of **hypercholesterolemia.**
AU Uusitupa M; Ebeling T; Happonen P; Voutilainen E; Turtola H; Parviainen M; Pyorala K
CS Department of Medicine, University of Kuopio, Finland.
SO JOURNAL OF CARDIOVASCULAR PHARMACOLOGY, **(1991 Oct)** 18 (4) 496-503.
Journal code: K78; 7902492. ISSN: 0160-2446.
CY United States
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LA English
FS Priority Journals
EM 199204
ED Entered STN: 19920424
Last Updated on STN: 19960129
Entered Medline: 19920407
AB Sixty-two patients (34 men and 28 women) aged 19-64 years, half of whom had familial **hypercholesterolemia,** treated initially for 18 weeks with **lovastatin** alone were randomly allocated either to **lovastatin** (L) and **cholestyramine** (16 g/day) or **lovastatin** and guar gum (L + GG 20 g/day) treatment for 18 additional weeks to compare the **hypocholesterolemic** effects of these two combination therapies. The patients were selected for this study from a larger study of patients (n = 120) with severe **hypercholesterolemia** [serum total **cholesterol** (serum Chol) 6.5-16.3 mM before treatment], and only those patients in whom serum Chol after **lovastatin** alone (dose 80 mg/day) remained greater than or equal to 5.2 mM were eligible for evaluation of combination therapies. Serum Chol decreased from 10.6 +/- 1.6 to 5.9 +/- 1.3 mM (mean +/- SD) (p less than 0.001) and low-density lipoprotein **cholesterol** (LDL Chol) from 8.5 +/- 1.8 to 4.1 +/- 1 mM (p less than 0.001) in patients treated with L + GG (values before the beginning of **lovastatin** and at the end of the combination therapy). The respective changes were from 10.9 +/- 2.2 to 5.5 +/- 1.2 mM (p less than 0.001) and from 8.7 +/- 2.3 to 3.5 +/- 1.2 mM (p less than 0.001) in patients treated with **lovastatin** and **cholestyramine** (L + C). At the end of the study, both serum Chol (p less than 0.005) and LDL Chol (p less than 0.01) were significantly lower with L + C than with L + GG.(ABSTRACT TRUNCATED AT 250 WORDS)
CT Check Tags: Comparative Study; Female; Human; Male; Support, Non-U.S. Gov't
Adult
Aged
Apolipoprotein A-I: ME, metabolism
Apolipoproteins B: ME, metabolism
Blood Pressure: DE, drug effects
Body Weight: DE, drug effects
Cholestyramine: AD, administration & dosage

Cholestyramine: AE, adverse effects
***Cholestyramine: TU, therapeutic use**
Double-Blind Method
Drug Therapy, Combination
Galactans: AD, administration & dosage
Galactans: AE, adverse effects
***Galactans: TU, therapeutic use**
Hypercholesterolemia: BL, blood
***Hypercholesterolemia: DT, drug therapy**
Hypercholesterolemia, Familial: BL, blood
Hypercholesterolemia, Familial: DT, drug therapy
Lipids: BL, blood
Lovastatin: AD, administration & dosage
Lovastatin: AE, adverse effects
***Lovastatin: TU, therapeutic use**
Mannans: AD, administration & dosage
Mannans: AE, adverse effects
***Mannans: TU, therapeutic use**
Middle Age
RN **11041-12-6 (Cholestyramine); 75330-75-5 (Lovastatin);** 9000-30-0 (guar gum)
CN 0 (Apolipoprotein A-I); 0 (Apolipoproteins B); 0 (Galactans); 0 (Lipids); 0 (Mannans)

L173 ANSWER 23 OF 63 MEDLINE
AN 92162100 MEDLINE
DN 92162100 PubMed ID: 1789813
TI Long-term efficacy and safety of simvastatin alone and in combination therapy in treatment of **hypercholesterolaemia.**
AU Molgaard J; Lundh B L; von Schenck H; Olsson A G
CS Department of Internal Medicine, Faculty of Health Sciences, University Hospital, Linkoping, Sweden.
SO ATHEROSCLEROSIS, **(1991 Dec)** 91 Suppl S21-8.
Journal code: 95X; 0242543. ISSN: 0021-9150.
CY Netherlands
DT (CLINICAL TRIAL)
(CONTROLLED CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199203
ED Entered STN: 19920410
Last Updated on STN: 19980206
Entered Medline: 19920325
AB The 3-years efficacy and safety of the 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitor simvastatin (S) (previously called synvinolin or MK-733) has been studied in single and combined therapy with **cholestyramine** (C) in 48 **hypercholesterolaemic** patients. Plasma lipids, lipoproteins and apolipoproteins A-I and B, and blood safety tests (haematology, liver function, creatine phosphokinase (CPK), creatinine, blood glucose and thyroid function) were determined regularly throughout the study. Extensive ophthalmological examinations with particular focus on the lens were done before initiation of therapy and at every 6 months during drug treatment. Maximal reductions of mean plasma total **cholesterol** concentration (34% with S; 47% with S + C) and low-density lipoprotein (LDL)-**cholesterol** concentration (42% with S; 56% with S + C) were achieved after 4 weeks on full-dose therapy. During continued treatment, years 1 through 3, the reduction of mean plasma total **cholesterol** was 26-29% with S alone, and 31-41% with S + C. Significant reductions of plasma triglycerides (15-27%) and very low density lipoprotein (VLDL) triglycerides (10-27%) were achieved in the group treated with S as single therapy. In this group there was also a significant increase (10-14%) of high-density lipoprotein (HDL)-**cholesterol**. In liver aspartate (AST) and alanine (ALT) aminotransferases, as well as alkaline phosphatase (ALP), minor and variable, but usually transient, increases were seen. Repeated

ophthalmological examinations did not demonstrate any drug-related side effects. It is concluded that simvastatin is a safe and efficient **cholesterol**-lowering drug for long-term therapy, both as a single drug and in combination with **cholestyramine**.

CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't
Adult
Aged
***Anticholesteremic Agents: AD, administration & dosage**
Anticholesteremic Agents: AE, adverse effects
Cholestyramine: TU, therapeutic use
Clinical Trials
Drug Therapy, Combination
*Hydroxymethylglutaryl CoA Reductases: AI, antagonists & inhibitors
Hypercholesterolemia: BL, blood
***Hypercholesterolemia: DT, drug therapy**
Lens, Crystalline: DE, drug effects
Lipids: BL, blood
Liver: DE, drug effects
Lovastatin: AD, administration & dosage
Lovastatin: AE, adverse effects
***Lovastatin: AA, analogs & derivatives**
Middle Age
Simvastatin

RN **11041-12-6 (Cholestyramine); 75330-75-5 (Lovastatin);** 79902-63-9 (Simvastatin)

CN 0 (**Anticholesteremic** Agents); 0 (Lipids); EC 1.1.1.88 (Hydroxymethylglutaryl CoA Reductases)

L173 ANSWER 24 OF 63 MEDLINE

AN 92152564 MEDLINE

DN 92152564 PubMed ID: 1785747

TI [Study of LDL receptors and response to **lovastatin** therapy in familial homozygotic **hypercholesterolemia**].
Estudio de receptores del colesterol LDL y respuesta del tratamiento con **lovastatina** en la hipercolesterolemia familiar homocigota.

AU Ausina Gomez A; Gilsanz Peral A; Montero Brens C; Dalmau Serra J

CS Unidad de Nutricion, Hospital Infantil La Fe, Valencia.

SO ANALES ESPANOLES DE PEDIATRIA, **(1991 Nov)** 35 (5) 327-31. Ref: 18
Journal code: 49N; 0420463. ISSN: 0302-4342.

CY Spain

DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)

LA Spanish

FS Priority Journals

EM 199203

ED Entered STN: 19920405
Last Updated on STN: 19920405
Entered Medline: 19920319

AB This study shows the results obtained with **lovastatin** as a combined therapy with probucol and **cholestyramine** on the lipid profile of two patients with homozygous familial **hypercholesterolemia**. Both have been diagnosed according to the clinical and biochemical criteria (tipe IIa **hypercholesterolemia**) as well as by the **cholesterol** or low density lipoprotein (LDL-C) receptor analysis. After the initial probucol and **cholestyramine** treatment we observed a drop of total **cholesterol** (T-C) of 41.7% and 46% as well as LDL-C of 51.6% and 49.3% in both patients. Respectively when **lovastatin** were associated an additional drop of T-C of 23.7%, LDL-C of 23.2%, high-density lipoprotein **cholesterol** (HDL-C) of 22.4% and the apoprotein B (Apo B) of 37% were obtained in one patient (receptor-defective) but no change in the lipid profile were obtained in the other patient (receptor-negative). No adverse effects were observed with this drug. This drug could be of help as a combined therapy in the

treatment of homozygous familial **hypercholesterolemia**, even though the treatment of choice is the LDL-plasma feresis and/or liver transplantation. We expound the difficulties relate to LDL receptor study in homocygous receptor-negative patients.

CT Check Tags: Human
Cholestyramine: TU, therapeutic use
Drug Therapy, Combination
Homozygote
***Hypercholesterolemia, Familial: DT, drug therapy**
Hypercholesterolemia, Familial: GE, genetics
***Lovastatin: TU, therapeutic use**
*Receptors, LDL: DE, drug effects

RN **11041-12-6 (Cholestyramine); 75330-75-5 (Lovastatin)**

CN 0 (Receptors, LDL)

L173 ANSWER 25 OF 63 MEDLINE

AN 92017348 MEDLINE

DN 92017348 PubMed ID: 1921811

TI Treatment of primary **hypercholesterolaemia** with simvastatin. New Zealand multicentre evaluation.

AU Lintott C J; Scott R S; Sharpe D N; Nye E R; Charleson H; French J K; White H D; Reuben S; Maling T J; Lewis G R; +

CS Princess Margaret Hospital, Christchurch, New Zealand.

SO MEDICAL JOURNAL OF AUSTRALIA, **(1991 Oct 7)** 155 (7) 433-6.
Journal code: M26; 0400714. ISSN: 0025-729X.

CY Australia

DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)

LA English

FS Priority Journals

EM 199111

ED Entered STN: 19920124
Last Updated on STN: 19980206
Entered Medline: 19911107

AB OBJECTIVE: To assess the efficacy of simvastatin in a large patient cohort. DESIGN: In an open multicentre study, after a four week placebo phase, patients were treated with simvastatin for 24 weeks; a subgroup continued therapy for a further 24 weeks. Efficacy of simvastatin (a) with prolonged use over three years, and (b) in combination with bezafibrate was assessed in an open single site study. SETTING: Lipid or cardiology specialist hospital outpatient clinics. PATIENTS: For the open multicentre study, 228 patients with primary **hypercholesterolaemia** (total **cholesterol** level greater than 6.5 mmol/L) were recruited, of whom 224 met entry criteria and completed the study. Forty-seven of these patients continued therapy for one year. In the open single site study, 22 patients (with low density lipoprotein [LDL] **cholesterol** levels greater than 4.3 mmol/L) participated in studies of long term use (n = 9) or of combined therapy (n = 13). INTERVENTION: Therapy in the open multicentre study began with 10 mg of simvastatin per day, doubling to 20 mg after six weeks and then 40 mg after 12 weeks of therapy if total **cholesterol** levels persisted above 5.2 mmol/L. In the study of long term use, simvastatin (40 mg daily) was taken continuously over three years. In the study of combination therapy, bezafibrate (600 mg daily) was taken in addition to simvastatin (40 mg daily) for 10 months. MAIN OUTCOME MEASURES: Plasma lipid and lipoprotein concentrations. RESULTS: In the multicentre study, total plasma **cholesterol** levels were reduced by 32.8% from 9.11 +/- 1.84 (in mmol/L, mean +/- SD) to 6.12 +/- 1.25 (P less than 0.001), and LDL **cholesterol** levels by 41.4% from 6.90 +/- 1.92 to 4.04 +/- 0.31 (P less than 0.001). The effect of therapy was sustained in those patients continuing therapy to 48 weeks. The study of long term use found no significant attenuation of effect over three years of monotherapy. Combined simvastatin/bezafibrate therapy reduced the LDL **cholesterol** concentration by a further 19.9% (P less than 0.001) from levels achieved on simvastatin alone. CONCLUSIONS: Simvastatin is an effective, well tolerated lipid lowering drug, without significant

attenuation of effect with prolonged use. Simvastatin plus bezafibrate appears to be a potentially useful drug combination.

CT Check Tags: Female; Human; Male
Adult
Aged
Anticholesteremic Agents: AE, adverse effects
***Anticholesteremic Agents: TU, therapeutic use**
Bezafibrate: TU, therapeutic use
Cholesterol: BL, blood
Cohort Studies
Drug Therapy, Combination
Hypercholesterolemia: BL, blood
***Hypercholesterolemia: DT, drug therapy**
Lipoproteins, LDL Cholesterol: BL, blood
Lovastatin: AE, adverse effects
***Lovastatin: AA, analogs & derivatives**
Lovastatin: TU, therapeutic use
Middle Age
New Zealand
Simvastatin

RN 41859-67-0 (Bezafibrate); **57-88-5 (Cholesterol)**; **75330-75-5 (Lovastatin)**; 79902-63-9 (Simvastatin)

CN 0 (**Anticholesteremic** Agents); 0 (Lipoproteins, LDL **Cholesterol**)

L173 ANSWER 26 OF 63 MEDLINE

AN 91349303 MEDLINE

DN 91349303 PubMed ID: 1880219

TI Lecithin: **cholesterol** acyltransferase activity in familial **hypercholesterolemia** treated with simvastatin and simvastatin plus low-dose colestipol.

AU Desager J P; Horsmans Y; Harvengt C

CS Laboratoire de Pharmacotherapie, Universite Catholique de Louvain, Brussels, Belgium.

SO JOURNAL OF CLINICAL PHARMACOLOGY, **(1991 Jun)** 31 (6) 537-42.
Journal code: HT9; 0366372. ISSN: 0091-2700.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199110

ED Entered STN: 19911020
Last Updated on STN: 19980206
Entered Medline: 19911003

AB In 19 patients with heterozygous familial **hypercholesterolemia** (FH), the effects of simvastatin (S) 20 mg/d, 40 mg/d, and 40 mg/d plus low-dose colestipol (10 g/d) on plasma lipids, plasma lipoproteins, and plasma lecithin: **cholesterol** acyltransferase (LCAT) activity were investigated after an original dose-range escalation/descalation design. The drug regimen was changed every 8 weeks. A significant reduction in total **cholesterol** and LDL-**cholesterol** was observed, reaching 39% and 54% for the drug combination (week 28), and total apoprotein B and LDL-apoprotein B were reduced by 39% and 50%, respectively. Triglycerides were significantly lowered by S alone (up to 29% with 40 mg/d). HDL-**cholesterol** increased during therapy but the **cholesterol** content in HDL2-HDL3 fractions (isolated by ultracentrifugation) did not change significantly during the different steps. The ratio LDL-C/HDL-C fell by 57% at week 28. Plasma LCAT activity expressed as FER was significantly enhanced by S alone (+33%), and a further increase on drug combination regimen (+58%) was observed. This effect could be considered as a consequence of the increased fractional clearance of LDL-C. It tended to be sustained during the descalation part of the study. Biochemical adverse effects were scarce and transient. In conclusion, the combination therapy increased the plasma LCAT/FER activity without a preferential enhancement in HDL2-C concentration. This original design allowed to define the most appropriate individual

cholesterol-lowering drug dosage in FH patients.
CT Check Tags: Comparative Study; Female; Human; Male; Support, Non-U.S. Gov't
Adolescence
Adult
Anticholesteremic Agents: AD, administration & dosage
***Anticholesteremic Agents: TU, therapeutic use**
Colestipol: AD, administration & dosage
*Colestipol: TU, therapeutic use
Drug Therapy, Combination
***Hypercholesterolemia, Familial: BL, blood**
Hypercholesterolemia, Familial: DT, drug therapy
Hypercholesterolemia, Familial: EN, enzymology
Lovastatin: AD, administration & dosage
***Lovastatin: AA, analogs & derivatives**
Lovastatin: TU, therapeutic use
Middle Age
*Phosphatidylcholine-Sterol O-Acyltransferase: BL, blood
Phosphatidylcholine-Sterol O-Acyltransferase: ME, metabolism
Simvastatin
RN 50925-79-6 (Colestipol); **75330-75-5 (Lovastatin)**; 79902-63-9 (Simvastatin)
CN 0 (**Anticholesteremic** Agents); EC 2.3.1.43 (Phosphatidylcholine-Sterol O-Acyltransferase)

L173 ANSWER 27 OF 63 MEDLINE
AN 91262174 MEDLINE
DN 91262174 PubMed ID: 2047557
TI [Treatment of **hypercholesterolemic** patients of different age with simvastatin: 1-year study].
Trattamento di pazienti ipercolesterolemici di diversa eta con simvastatina. Studio di un anno.
AU Pernigotti L; Bo M; Poli L; Zanocchi M; Fiandra U; Pedrazzini V; Fabris F
CS Istituto di Medicina e Chirurgia geriatrica, Ospedale Molinette, Universita, Torino.
SO RECENTI PROGRESSI IN MEDICINA, **(1991 Mar)** 82 (3) 155-62.
Journal code: R1T; 0401271. ISSN: 0034-1193.
CY Italy
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LA Italian
FS Priority Journals
EM 199107
ED Entered STN: 19910802
Last Updated on STN: 19980206
Entered Medline: 19910718
AB Nowadays there is no direct evidence that lowering **cholesterol** may reduce the CHD in the elderly; however, several evidences suggest the potential benefit of a dietetic and/or pharmacologic intervention in healthy young-old **hypercholesterolemics**. In this study we evaluated the efficacy and tolerability of simvastatin, alone or in combination with **cholestyramine**, in two groups of patients (group A: age 30-55 years and group B: age 60-75 years) with primary **hypercholesterolemia**, over a 48-week period. In both groups Simvastatin induced a significant reduction in total and LDL **cholesterol** (p less than 0.001 both), with a decrease of the total/HDL **cholesterol** ratio (p less than 0.001). A reduction of the apo-B100 levels was also observed (respectively p less than 0.01 and p less than 0.001) with a significant improvement of the apo-B100/apo-A1 ratio (p less than 0.01). Simvastatin was well tolerated and free of remarkable side effects in both groups.
CT Check Tags: Comparative Study; Human
Adult
Age Factors
Aged
Anticholesteremic Agents: AD, administration & dosage

***Anticholesteremic Agents: TU, therapeutic use**
Cholesterol: BL, blood
Cholestyramine: AD, administration & dosage
Drug Therapy, Combination
*Hydroxymethylglutaryl CoA Reductases: AI, antagonists & inhibitors
Hypercholesterolemia: BL, blood
***Hypercholesterolemia: DT, drug therapy**
Lipoproteins, LDL Cholesterol: BL, blood
Lovastatin: AD, administration & dosage
***Lovastatin: AA, analogs & derivatives**
Lovastatin: TU, therapeutic use
Middle Age
Simvastatin
Time Factors
RN **11041-12-6 (Cholestyramine); 57-88-5 (Cholesterol); 75330-75-5 (Lovastatin);** 79902-63-9 (Simvastatin)
CN 0 (**Anticholesteremic** Agents); 0 (Lipoproteins, LDL **Cholesterol**); EC 1.1.1.88 (Hydroxymethylglutaryl CoA Reductases)

L173 ANSWER 28 OF 63 MEDLINE
AN 91160023 MEDLINE
DN 91160023 PubMed ID: 2073670
TI Combination drug therapy with HMG CoA reductase inhibitors and bile acid sequestrants for **hypercholesterolemia.**
AU Erkelens D W
CS University Hospital, Utrecht, The Netherlands.
SO CARDIOLOGY, **(1990)** 77 Suppl 4 33-8.
Journal code: COI; 1266406. ISSN: 0008-6312.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199104
ED Entered STN: 19910505
Last Updated on STN: 19980206
Entered Medline: 19910416
AB Single-drug therapy is often not sufficient to lower total and low-density lipoprotein (LDL) **cholesterol** levels in patients with familial **hypercholesterolemia** to desirable or target levels. Therefore, combination drug therapy is often necessary. The most potent therapy to achieve this goal is a combination of a 3-hydroxy-3-methylglutaryl coenzyme A (HMG CoA) reductase inhibitor, which reduces **cholesterol** synthesis, and a bile acid sequestrant, which indirectly depletes the intrahepatic **cholesterol** pool. LDL **cholesterol** reductions reportedly vary between 52 and 54% in short-term trials. Combining a bile acid sequestrant with nicotinic acid reduces LDL **cholesterol** 34-55%, and with a fibrate, 12-42%. The triple-drug regimen of bile acid sequestrant, an HMG CoA reductase inhibitor, and nicotinic acid is even more effective, achieving reductions of 59-67%. All these regimens elevate high-density lipoprotein **cholesterol** levels concomitantly by 2-37%.
CT Check Tags: Human
***Cholestyramine: AD, administration & dosage**
Cholestyramine: TU, therapeutic use
Drug Therapy, Combination
Hydroxymethylglutaryl CoA Reductases: AD, administration & dosage
*Hydroxymethylglutaryl CoA Reductases: AI, antagonists & inhibitors
Hypercholesterolemia, Familial: BL, blood
***Hypercholesterolemia, Familial: DT, drug therapy**
Lipids: BL, blood
Lovastatin: AD, administration & dosage
Lovastatin: AA, analogs & derivatives
Lovastatin: TU, therapeutic use
Niacin: AD, administration & dosage
Niacin: TU, therapeutic use
Simvastatin

RN **11041-12-6 (Cholestyramine)**; 59-67-6 (Niacin); **75330-75-5 (Lovastatin)**; 79902-63-9 (Simvastatin)
CN 0 (Lipids); EC 1.1.1.88 (Hydroxymethylglutaryl CoA Reductases)

L173 ANSWER 29 OF 63 MEDLINE
AN 91138290 MEDLINE
DN 91138290 PubMed ID: 2149540
TI [The treatment of refractory hyperlipoproteinemias].
Il trattamento delle iperlipoproteinemie resistenti.
AU Barone A; Ansuini R; Francolini G; Frausini G; Pupita F
CS Divisione di Medicina Interna, Ospedale Unificato di Fano-Mondolfo.
SO CLINICA TERAPEUTICA, **(1990 Oct 15)** 135 (1) 31-6.
Journal code: DKN; 0372604. ISSN: 0009-9074.
CY Italy
DT Journal; Article; (JOURNAL ARTICLE)
LA Italian
FS Priority Journals
EM 199103
ED Entered STN: 19910412
Last Updated on STN: 19980206
Entered Medline: 19910327
AB The authors have studied a group of 25 patients treated with an HMG-CoA reductase inhibitor associated with DEAE-dextran, a safe and useful drug for the treatment of dyslipidemia. The patients were selected from a group of subjects previously submitted to long-term treatment with an HMG-CoA reductase inhibitor only who had failed to achieve normal **cholesterol** blood levels. The combined treatment with DEAE-dextran (1.5 g 3 times daily) and simvastatin (20 mg once daily) for 90 days lead to a further significant decrease in **cholesterol** and triglyceride blood levels. These findings confirm the validity of the association of an ion exchange resin with an HMG-CoA reductase inhibitor in the treatment of refractory dyslipidemias.
CT Check Tags: Female; Human; Male
Anticholesteremic Agents: TU, therapeutic use
Cholesterol: BL, blood
DEAE-Dextran: TU, therapeutic use
Drug Evaluation
Drug Therapy, Combination
Hyperlipoproteinemia: BL, blood
***Hyperlipoproteinemia: DT, drug therapy**
Lovastatin: AA, analogs & derivatives
Lovastatin: TU, therapeutic use
Middle Age
Simvastatin
Triglycerides: BL, blood
RN **57-88-5 (Cholesterol)**; **75330-75-5 (Lovastatin)**; 79902-63-9 (Simvastatin); 9015-73-0 (DEAE-Dextran)
CN 0 (**Anticholesteremic** Agents); 0 (Triglycerides)

L173 ANSWER 30 OF 63 MEDLINE
AN 91069076 MEDLINE
DN 91069076 PubMed ID: 2252289
TI [Homozygous familial **hypercholesterolemia**. Response to combined **cholestyramine** and **lovastatin** therapy].
Hipercolesterolemia familiar homocigota. Respuesta al tratamiento combinado con colestiramina y **lovastatina**.
AU Obando Santaella I; Fernandez Gomez E; Mongil Ruiz I; Escobar Gallego A; Garcia Alegria J J; Gascon Luna F; Masana Marin L
CS Servicio de Pediatria, Hospital G B de Pozoblanco, Cordoba.
SO ANALES ESPANOLES DE PEDIATRIA, **(1990 Jul)** 33 (1) 58-60.
Journal code: 49N; 0420463. ISSN: 0302-4342.
CY Spain
DT Journal; Article; (JOURNAL ARTICLE)
LA Spanish
FS Priority Journals
EM 199101

ED Entered STN: 19910308
Last Updated on STN: 19910308
Entered Medline: 19910117
AB Homozygous familiar **hypercholesterolemia** (FH) is a serious inherited disease caused by a genetic defect in the cell surface receptor that controls the degradation of low density lipoprotein (LDL). These patients often have myocardial infarction in their teens or early adulthood and are usually unresponsive to drugs. Recently it has been reported promising results using combined drugs regimens in patients with residual receptor activity. We report a new additional patient with receptor-defective homozygous FH treated with a combination of **lovastatin** and **cholestyramine**. The **cholesterol** levels were reduced in a 67% and there were adverse events related to treatment during a 7 month period of follow-up.
CT Check Tags: Case Report; Human; Male
Child, Preschool
***Cholestyramine: TU, therapeutic use**
Drug Therapy, Combination
Homozygote
Hypercholesterolemia, Familial: DT, drug therapy
***Hypercholesterolemia, Familial: GE, genetics**
***Lovastatin: TU, therapeutic use**
RN **11041-12-6 (Cholestyramine); 75330-75-5 (Lovastatin)**

L173 ANSWER 31 OF 63 MEDLINE
AN 91056652 MEDLINE
DN 91056652 PubMed ID: 2123013
TI Reducing high blood **cholesterol** level with drugs. Cost-effectiveness of pharmacologic management.
CM Comment in: JAMA. 1991 Apr 17;265(15):1949-50
AU Schulman K A; Kinosian B; Jacobson T A; Glick H; Willian M K; Koffer H; Eisenberg J M
CS Department of Medicine, Robert Wood Johnson Foundation Clinical Scholars Program, University of Pennsylvania, Philadelphia.
SO JAMA, **(1990 Dec 19)** 264 (23) 3025-33. Ref: 72
Journal code: KFR; 7501160. ISSN: 0098-7484.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199101
ED Entered STN: 19910222
Last Updated on STN: 19910222
Entered Medline: 19910103
AB We performed a cost-effectiveness analysis of pharmacologic treatment of high blood **cholesterol** levels. Agents modeled were **cholestyramine**, colestipol, gemfibrozil, **lovastatin**, niacin, and probucol. Pharmacologic effectiveness was estimated from reported studies. Cost estimates reflect societal resource consumption. Annual costs for therapy ranged from $327 (niacin) to $1881 (**lovastatin**, 80 mg/d). Niacin was the most efficient agent for reducing low-density lipoprotein **cholesterol** levels, having an average cost over 5 years of $139 per percent reduction in low-density lipoprotein **cholesterol** level. **Lovastatin** (20 mg/d) was also efficient ($177 per percent reduction). **Cholestyramine** was least efficient at $347. For high-density lipoprotein **cholesterol**, niacin was most efficient, at $116 per percent increase in high-density lipoprotein **cholesterol** level, followed by gemfibrozil at $271. Analyses combining low-density lipoprotein **cholesterol** and high-density lipoprotein **cholesterol** effects suggest that niacin and **lovastatin** (20 mg/d) were most efficient for reducing cardiovascular risk.
CT Check Tags: Human; Support, Non-U.S. Gov't
***Anticholesteremic Agents: TU, therapeutic use**

Cholestyramine: TU, therapeutic use
Clinical Trials
Colestipol: TU, therapeutic use
Cost-Benefit Analysis
Drug Therapy, Combination
Gemfibrozil: TU, therapeutic use
Hypercholesterolemia: DT, drug therapy
***Hypercholesterolemia: EC, economics**
Lovastatin: TU, therapeutic use
Niacin: TU, therapeutic use
Probucol: TU, therapeutic use
Sensitivity and Specificity
RN **11041-12-6 (Cholestyramine)**; 23288-49-5 (Probucol); 25812-30-0 (Gemfibrozil); 50925-79-6 (Colestipol); 59-67-6 (Niacin); **75330-75-5 (Lovastatin)**
CN 0 (**Anticholesteremic** Agents)

L173 ANSWER 32 OF 63 MEDLINE
AN 91056649 MEDLINE
DN 91056649 PubMed ID: 2243428
TI Regression of coronary atherosclerosis during treatment of familial **hypercholesterolemia** with combined drug regimens.
CM Comment in: JAMA. 1991 Apr 3;265(13):1688-9
AU Kane J P; Malloy M J; Ports T A; Phillips N R; Diehl J C; Havel R J
CS Cardiovascular Research Institute, University of California, San Francisco 94143-0130.
NC 5 MO1 RR00079 (NCRR)
HL 14237 (NHLBI)
SO JAMA, **(1990 Dec 19)** 264 (23) 3007-12.
Journal code: KFR; 7501160. ISSN: 0098-7484.
CY United States
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199101
ED Entered STN: 19910222
Last Updated on STN: 19910222
Entered Medline: 19910103
AB We conducted a randomized, controlled trial in 72 patients with heterozygous familial **hypercholesterolemia** to test whether reducing plasma low-density lipoprotein levels by diet and combined drug regimens can induce regression of coronary lesions. Four hundred fifty-seven lesions were measured before and after a 26-month interval by computer-based quantitative angiography. The primary outcome variable was within-patient mean change in percent area stenosis. Mean low-density lipoprotein **cholesterol** levels decreased from 7.32 +/- 1.5 to 4.45 +/- 1.6 mmol/L. The mean change in percent area stenosis among controls was +0.80, indicating progression, while the mean change for the treatment group was -1.53, indicating regression (P = .039 by two-tailed t test for the difference between groups). Regression among women, analyzed separately, was also significant. The change in percent area stenosis was correlated with low-density lipoprotein levels on trial. We conclude that reduction of low-density lipoprotein **cholesterol** levels can induce regression of atherosclerotic lesions of the coronary arteries in patients with familial **hypercholesterolemia**. The anticipation of benefit from treatment applies to women and men alike.
CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Adult
Aged
Colestipol: AD, administration & dosage
Coronary Arteriosclerosis: BL, blood
Coronary Arteriosclerosis: DT, drug therapy
*Coronary Arteriosclerosis: RA, radiography

Drug Therapy, Combination
Hypercholesterolemia, Familial: BL, blood
***Hypercholesterolemia, Familial: DT, drug therapy**
Lipoproteins, HDL Cholesterol: BL, blood
Lipoproteins, LDL Cholesterol: BL, blood
Lovastatin: AD, administration & dosage
Middle Age
Niacin: AE, adverse effects
Radiographic Image Interpretation, Computer-Assisted
Triglycerides: BL, blood
RN 50925-79-6 (Colestipol); 59-67-6 (Niacin); **75330-75-5 (Lovastatin)**
CN 0 (Lipoproteins, HDL **Cholesterol**); 0 (Lipoproteins, LDL **Cholesterol**); 0 (Triglycerides)

L173 ANSWER 33 OF 63 MEDLINE
AN 90385302 MEDLINE
DN 90385302 PubMed ID: 2402652
TI Regression of tendon xanthomas in patients with familial **hypercholesterolemia** treated with **lovastatin**.
AU Illingworth D R; Cope R; Bacon S P
CS Department of Medicine, Oregon Health Sciences University, Portland 97201-3098.
NC HL32271 (NHLBI)
HL37940 (NHLBI)
RR334 (NCRR)
SO SOUTHERN MEDICAL JOURNAL, **(1990 Sep)** 83 (9) 1053-7.
Journal code: UVH; 0404522. ISSN: 0038-4348.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199010
ED Entered STN: 19901122
Last Updated on STN: 19901122
Entered Medline: 19901019
AB Plasma concentrations of total and low-density lipoprotein **cholesterol** are increased twofold to threefold in patients with heterozygous familial **hypercholesterolemia**. This sustained increase leads to accelerated rates of **cholesterol** deposition in the coronary arteries and to the development of tendon xanthomas. To assess whether hypolipidemic therapy with **lovastatin**, alone and in combination therapy with colestipol hydrochloride or nicotinic acid, results in regression of lipid deposits in the tendons of these patients, we have measured Achilles tendon diameters by xeroradiography before and after treatment. In 20 patients treated for a mean of 43 months (during which time plasma **cholesterol** concentrations decreased from 430 to 247 mg/dL), the diameter of both the left and right Achilles tendons measured at three different locations decreased by 0.55 to 1.5 mm. Larger reductions were seen in the tendons of seven of these patients who were treated for a mean of 64 months and whose mean concentrations of **cholesterol** fell from 488 to 279 mg/dL. We conclude that effective long-term hypolipidemic therapy leads to diminution in the size of Achilles tendon xanthomas in patients with heterozygous familial **hypercholesterolemia** and that such therapy is associated with mobilization of tissue stores of **cholesterol** in these patients.
CT Check Tags: Female; Human; Male; Support, U.S. Gov't, P.H.S.
Achilles Tendon: DE, drug effects
Achilles Tendon: RA, radiography
Adult
Colestipol: TU, therapeutic use
Drug Therapy, Combination
***Hypercholesterolemia, Familial: DT, drug therapy**
Lipoproteins, LDL Cholesterol: BL, blood
***Lovastatin: TU, therapeutic use**
Middle Age
Niacin: TU, therapeutic use

Remission Induction
Tendons, Para-Articular: PA, pathology
*Wolman Disease: DT, drug therapy
Wolman Disease: RA, radiography
RN 50925-79-6 (Colestipol); 59-67-6 (Niacin); **75330-75-5 (Lovastatin)**
CN 0 (Lipoproteins, LDL **Cholesterol**)

L173 ANSWER 34 OF 63 MEDLINE
AN 90340166 MEDLINE
DN 90340166 PubMed ID: 2199801
TI Comparison of simvastatin and **cholestyramine** in the treatment of primary **hypercholesterolaemia.**
CM Erratum in: Med J Aust 1991 Feb 18;154(4):296
AU O'Brien R C; Simons L A; Clifton P; Cooper M E; Jennings G L; Jerums G; Nestel P J; Sullivan D
CS Department of Medicine, Austin Hospital, Heidelberg, VIC.
SO MEDICAL JOURNAL OF AUSTRALIA, **(1990 May 7)** 152 (9) 480-3.
Journal code: M26; 0400714. ISSN: 0025-729X.
CY Australia
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
(RANDOMIZED CONTROLLED TRIAL)
LA English
FS Priority Journals
EM 199009
ED Entered STN: 19901012
Last Updated on STN: 19980206
Entered Medline: 19900907
AB The effects of simvastatin, a competitive inhibitor of the enzyme 3-hydroxy-3-methylglutaryl-coenzyme A reductase, on plasma lipid levels were compared with those of the bile acid sequestrant **cholestyramine** in a randomized parallel study of 60 subjects with primary **hypercholesterolaemia**. After a 12-week direct comparison period 37 subjects with inadequate **cholesterol** reduction received a combination of both drugs and all subjects were followed for a further 40 weeks. Simvastatin was more effective than **cholestyramine** in lowering total and LDL **cholesterol** levels and the LDL/HDL ratio (-31.7% v. -19.7% [P less than 0.01], -41.0% v. -31.8% [P less than 0.05] and -46.7% v. -33.6% [P less than 0.01], respectively at Week 12). Only simvastatin significantly increased the HDL **cholesterol** concentration (+13.3% [P less than 0.01] v. +6.4%). **Cholestyramine** increased plasma triglyceride levels by 37.5% (P less than 0.01) whereas simvastatin caused a slight non-significant reduction. Combined therapy produced a further decrease in total and LDL **cholesterol** levels, and in the LDL/HDL ratio, which was sustained for the duration of the study. Simvastatin was better tolerated than **cholestyramine** (P less than 0.01), and combining the two drugs enhanced efficacy without increasing the frequency of side effects.
CT Check Tags: Comparative Study; Female; Human; Male; Support, Non-U.S. Gov't
Adult
Aged
Analysis of Variance
Anticholesteremic Agents: AD, administration & dosage
***Anticholesteremic Agents: TU, therapeutic use**
Australia
Cholesterol: BL, blood
Cholestyramine: AD, administration & dosage
***Cholestyramine: TU, therapeutic use**
Drug Therapy, Combination
Follow-Up Studies
Hydroxymethylglutaryl CoA Reductases: AI, antagonists & inhibitors
Hypercholesterolemia: BL, blood
***Hypercholesterolemia: DT, drug therapy**
Hypercholesterolemia: EN, enzymology

Lovastatin: AD, administration & dosage
***Lovastatin: AA, analogs & derivatives**
Lovastatin: TU, therapeutic use
Middle Age
Multicenter Studies
Randomized Controlled Trials
Simvastatin
Triglycerides: ~~BL, blood~~
RN **11041-12-6 (Cholestyramine)**; **57-88-5 (Cholesterol)**; **75330-75-5 (Lovastatin)**; 79902-63-9 (Simvastatin)
CN 0 (**Anticholesteremic** Agents); 0 (Triglycerides); EC 1.1.1.88 (Hydroxymethylglutaryl CoA Reductases)

sequestrant

L173 ANSWER 35 OF 63 MEDLINE
AN 90287319 MEDLINE
DN 90287319 PubMed ID: 2355995
TI The effects of simvastatin on serum lipoproteins in severe **hypercholesterolaemia**.
AU Mol M J; Stuyt P M; Demacker P N; Stalenhoef A F
CS Department of Medicine, University Hospital, Nijmegen.
SO NETHERLANDS JOURNAL OF MEDICINE, **(1990 Apr)** 36 (3-4) 182-90.
Journal code: NWY; 0356133. ISSN: 0300-2977.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199007
ED Entered STN: 19900824
Last Updated on STN: 19980206
Entered Medline: 19900724
AB The effects of simvastatin, an inhibitor of **cholesterol** synthesis, on serum lipids, lipoprotein composition and apolipoproteins were evaluated in a total of 50 patients with **hypercholesterolaemia**. In the first study, 24 patients (mean serum **cholesterol** 10.74 +/- 1.59 mmol/l) were treated with simvastatin 40 mg daily for 24 wk. Serum **cholesterol** and low density lipoprotein (LDL) **cholesterol** decreased to average values 29-36% and 35-42% below the basal value, respectively. Serum triglycerides decreased by 16-28%, and high density lipoprotein (HDL) **cholesterol** increased by 6-11%. Apolipoprotein A-I concentration increased 6-8% and that of apolipoprotein B decreased 29-33%. The composition of LDL remained unchanged whereas the very low density lipoproteins became enriched in triglycerides. Lipoprotein Lp(a) was not affected. In the second study 26 patients (mean serum **cholesterol** 12.35 +/- 2.05 mmol/l) were treated with simvastatin 40 mg daily as monotherapy or combined with a bile acid binding resin for 2 yr. Serum **cholesterol** levels decreased to values which remained stable throughout the entire study period; after 2 yr this decrease amounted to 43%. Compared to monotherapy, combination therapy yielded a further 12% decrease of **cholesterol**. In the entire group, triglycerides decreased by 16% and HDL **cholesterol** increased by 9%. Side effects were limited to slight increases in alanine aminotransferase and creatine phosphokinase in some patients. Simvastatin appears to be an important asset in the treatment of **hypercholesterolaemia**.
CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't
Adult
Apolipoproteins: BL, blood
Cholesterol: BL, blood
Cholestyramine: TU, therapeutic use
Colestipol: TU, therapeutic use
Drug Therapy, Combination
*Hydroxymethylglutaryl CoA Reductases: AI, antagonists & inhibitors
***Hypercholesterolemia, Familial: DT, drug therapy**
*Lipoproteins: BL, blood
Lovastatin: AE, adverse effects
***Lovastatin: AA, analogs & derivatives**

Lovastatin: PD, pharmacology
Lovastatin: TU, therapeutic use
Middle Age
Simvastatin
Triglycerides: BL, blood
RN **11041-12-6 (Cholestyramine)**; 50925-79-6 (Colestipol); **57-88-5 (Cholesterol)**; **75330-75-5 (Lovastatin)**; 79902-63-9 (Simvastatin)
CN 0 (Apolipoproteins); 0 (Lipoproteins); 0 (Triglycerides); EC 1.1.1.88 (Hydroxymethylglutaryl CoA Reductases)

L173 ANSWER 36 OF 63 MEDLINE
AN 90286050 MEDLINE
DN 90286050 PubMed ID: 2355431
TI Myopathy and rhabdomyolysis associated with **lovastatin** -gemfibrozil combination therapy.
CM Comment in: JAMA. 1990 Dec 19;264(23):2991-2
AU Pierce L R; Wysowski D K; Gross T P
CS Division of Metabolism and Endocrine Drug Products, Food and Drug Administration, Rockville, MD 20857.
SO JAMA, **(1990 Jul 4)** 264 (1) 71-5.
Journal code: KFR; 7501160. ISSN: 0098-7484.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199007
ED Entered STN: 19900824
Last Updated on STN: 19900824
Entered Medline: 19900720
AB The Food and Drug Administration documents the receipt of 12 case reports of severe myopathy or rhabdomyolysis associated with concomitant use of **lovastatin** and gemfibrozil, including 10 voluntary postmarketing, and 2 required, reports. All patients had serum creatine kinase levels of more than 10,000 U/L, 4 tested showed myoglobinuria, and 5 had acute renal failure. The patients' symptoms resolved when both drugs were discontinued. For the first year of marketing of **lovastatin**, spontaneous reports of myopathy with documentation of creatine kinase level were reviewed for the use of **lovastatin**, gemfibrozil, and combination therapy. The median creatine kinase level in reports involving concomitant **lovastatin** and gemfibrozil use was 15,250 U/L, 20 times that in reports with gemfibrozil use alone and 30 times that in reports with **lovastatin** use alone. Because of the potential for severe myopathy and life-threatening rhabdomyolysis, and given alternative drug combinations for treating hyperlipoproteinemia, the use of **lovastatin** in combination with gemfibrozil is to be discouraged.
CT Check Tags: Case Report; Female; Human; Male
Adult
Aged
Creatine Kinase: BL, blood
Drug Interactions
Drug Therapy, Combination
Gemfibrozil: AD, administration & dosage
*Gemfibrozil: AE, adverse effects
Hypercholesterolemia: DT, drug therapy
Kidney Failure, Acute: CI, chemically induced
Lovastatin: AD, administration & dosage
***Lovastatin: AE, adverse effects**
Middle Age
Muscular Diseases: BL, blood
*Muscular Diseases: CI, chemically induced
Rhabdomyolysis: BL, blood
*Rhabdomyolysis: CI, chemically induced
RN 25812-30-0 (Gemfibrozil); **75330-75-5 (Lovastatin)**
CN EC 2.7.3.2 (Creatine Kinase)

L173 ANSWER 37 OF 63 MEDLINE
AN 90282586 MEDLINE
DN 90282586 PubMed ID: 2353864
TI Management of primary mixed hyperlipidemia with **lovastatin**.
AU Vega G L; Grundy S M
CS Department of Clinical Nutrition, University of Texas Southwestern Medical Center, Dallas 75235.
NC HL-29252 (NHLBI)
MO-1RR00633 (NCRR)
SO ARCHIVES OF INTERNAL MEDICINE, **(1990 Jun)** 150 (6) 1313-9.
Journal code: 7FS; 0372440. ISSN: 0003-9926.
CY United States
DT (CLINICAL TRIAL)
(CONTROLLED CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199007
ED Entered STN: 19900824
Last Updated on STN: 19970203
Entered Medline: 19900718
AB Many patients with high levels of serum total **cholesterol** have a concomitant elevation of serum triglyceride levels and thus have mixed hyperlipidemia. In this study, 13 patients with mixed hyperlipidemia were treated with the **cholesterol**-lowering drug **lovastatin** to determine its effectiveness. In 9 of these patients, **lovastatin** therapy used alone was compared with the drug combination of **lovastatin** and gemfibrozil. In the 13 patients, **lovastatin** therapy produced a 31% reduction in total **cholesterol** level and a 32% decrease in triglyceride levels compared with placebo. It lowered very-low-density plus intermediate-density lipoprotein **cholesterol** levels by 40%, low-density lipoprotein **cholesterol** levels by 36%, and total apolipoprotein B levels by 28%. Concentrations of high-density lipoprotein **cholesterol** and apolipoprotein A-I were unchanged, but total **cholesterol** (and low-density lipoprotein **cholesterol**)/high-density lipoprotein **cholesterol** ratios were markedly reduced. Compared with **lovastatin** alone, **lovastatin** plus gemfibrozil produced greater decreases in very-low-density plus intermediate-density lipoprotein **cholesterol** levels and an increase in high-density lipoprotein **cholesterol** levels, but, in view of the higher risk for severe myopathy with this combination, **lovastatin** used alone may be adequate therapy for many patients with mixed hyperlipidemia.
CT Check Tags: Comparative Study; Human; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.
Adult
Aged
Cholesterol: BL, blood
Drug Therapy, Combination
Gemfibrozil: TU, therapeutic use
***Hyperlipidemia: DT, drug therapy**
Lipoproteins, HDL Cholesterol: BL, blood
Lipoproteins, LDL Cholesterol: BL, blood
Lipoproteins, VLDL Cholesterol: BL, blood
***Lovastatin: TU, therapeutic use**
Middle Age
Triglycerides: BL, blood
RN 25812-30-0 (Gemfibrozil); **57-88-5 (Cholesterol)**; **75330-75-5 (Lovastatin)**
CN 0 (Lipoproteins, HDL **Cholesterol**); 0 (Lipoproteins, LDL **Cholesterol**); 0 (Lipoproteins, VLDL **Cholesterol**); 0 (Triglycerides)

L173 ANSWER 38 OF 63 MEDLINE
AN 90265885 MEDLINE
DN 90265885 PubMed ID: 2111917

TI HMG CoA reductase inhibitors as lipid-lowering agents: five years experience with **lovastatin** and an appraisal of simvastatin and pravastatin.
AU Maher V M; Thompson G R
CS MRC Lipoprotein Team, Hammersmith Hospital, London.
SO QUARTERLY JOURNAL OF MEDICINE, **(1990 Feb)** 74 (274) 165-75.
Journal code: QKZ; 0401027. ISSN: 0033-5622.
CY ENGLAND: United Kingdom
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199007
ED Entered STN: 19900810
Last Updated on STN: 19980206
Entered Medline: 19900703
AB The HMG CoA reductase inhibitors are the most effective drugs for treating **hypercholesterolaemia** currently available. They inhibit **cholesterol** synthesis and thus stimulate receptor-mediated uptake and degradation of low-density lipoprotein **cholesterol** by the liver. In 30 patients with severe **hypercholesterolaemia** administration of **lovastatin** alone or in combination with other lipid-lowering manoeuvres maintained reductions of 25 to 31 per cent in serum **cholesterol** over five years. The drug was easy to take and well tolerated, the only significant side effect being a reversible myopathy. Two similar compounds, simvastatin and pravastatin, exert comparable effects on serum lipids, including modest reductions in triglycerides and increases in high-density lipoprotein **cholesterol**. The use of these drugs seems likely to exert a beneficial effect on atherosclerosis.
CT Check Tags: Comparative Study; Female; Human; Male
Adult
Aged
***Anticholesteremic Agents: TU, therapeutic use**
Cholestyramine: TU, therapeutic use
Clinical Trials
Dose-Response Relationship, Drug
Drug Therapy, Combination
Heptanoic Acids: TU, therapeutic use
*Hydroxymethylglutaryl CoA Reductases: AI, antagonists & inhibitors
***Hypercholesterolemia: DT, drug therapy**
Hypercholesterolemia: GE, genetics
Lovastatin: AE, adverse effects
Lovastatin: AA, analogs & derivatives
Lovastatin: TU, therapeutic use
Middle Age
Naphthalenes: TU, therapeutic use
Phenotype
Pravastatin
Simvastatin
Time Factors
RN **11041-12-6 (Cholestyramine); 75330-75-5 (Lovastatin);** 79902-63-9 (Simvastatin); 81093-37-0 (Pravastatin)
CN 0 (**Anticholesteremic** Agents); 0 (Heptanoic Acids); 0 (Naphthalenes); EC 1.1.1.88 (Hydroxymethylglutaryl CoA Reductases)

L173 ANSWER 39 OF 63 MEDLINE
AN 90220330 MEDLINE
DN 90220330 PubMed ID: 2182974
TI The hypolipidemic effects of **lovastatin** and clofibrate alone and in combination in patients with type III hyperlipoproteinemia.
AU Illingworth D R; O'Malley J P
CS Department of Medicine, Oregon Health Sciences University, Portland 97201.
NC HL28399 (NHLBI)
HL37940 (NHLBI)
RR334 (NCRR)

SO METABOLISM: CLINICAL AND EXPERIMENTAL, **(1990 Apr)** 39 (4) 403-9.
Journal code: MUM; 0375267. ISSN: 0026-0495.
CY United States
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199005
ED Entered STN: 19900622
Last Updated on STN: 19900622
Entered Medline: 19900515
AB The hypolipidemic effects of **lovastatin** and clofibrate have been evaluated in 12 patients with type III hyperlipoproteinemia. In these patients plasma concentrations of total **cholesterol** decreased from 500 +/- 56 mg/dL (mean +/- SEM) at baseline to 278 +/- 23 mg/dL on **lovastatin** (20 mg twice daily), and were 299 +/- 15 mg/dL during treatment with clofibrate (1 g twice daily). Nine patients were treated sequentially with **lovastatin** at doses of 20 and 40 mg twice daily and clofibrate; in these patients total plasma **cholesterol** concentrations decreased from 549 +/- 67 mg/dL at baseline to 291 +/- 24 mg/dL on **lovastatin** (20 mg twice daily), 247 +/- 20 mg/dL (40 mg twice daily) and were 297 +/- 18 mg/dL on monotherapy with clofibrate. Concentrations of very-low-density lipoprotein (VLDL) **cholesterol** were similar on clofibrate and the higher dose of **lovastatin,** whereas concentrations of low-density lipoprotein (LDL) **cholesterol** were significantly lower on **lovastatin**. In six patients who remained hyperlipidemic on monotherapy with either drug, combination drug therapy with **lovastatin** (20 mg twice daily) plus clofibrate reduced plasma concentrations of total **cholesterol** from 635 +/- 79 mg/dL to 205 +/- 11 mg/dL. No patients were discontinued from single or combined drug therapy and no significant biochemical abnormalities were observed. The results of this study demonstrate the potential usefulness of **lovastatin** in the therapy of type III hyperlipoproteinemia and indicate that, in selected patients who remain **hypercholesterolemic** on monotherapy with either clofibrate or **lovastatin,** combination drug therapy with both of these drugs is effective in further reducing plasma concentrations of total, VLDL, and LDL **cholesterol**.(ABSTRACT TRUNCATED AT 250 WORDS)
CT Check Tags: Comparative Study; Female; Human; Male; Support, U.S. Gov't, P.H.S.
Adult
Aged
Cholesterol: BL, blood
Clinical Trials
***Clofibrate: TU, therapeutic use**
Drug Therapy, Combination
Follow-Up Studies
Hyperlipoproteinemia Type III: BL, blood
***Hyperlipoproteinemia Type III: DT, drug therapy**
Lipoproteins: BL, blood
***Lovastatin: TU, therapeutic use**
Middle Age
Time Factors
Triglycerides: BL, blood
RN **57-88-5 (Cholesterol)**; 637-07-0 (Clofibrate); **75330-75-5 (Lovastatin)**
CN 0 (Lipoproteins); 0 (Triglycerides)

L173 ANSWER 40 OF 63 MEDLINE
AN 90185518 MEDLINE
DN 90185518 PubMed ID: 2312032
TI [HMG-CoA reductase inhibitors in familial **hypercholesterolemia**. Therapy with simvastatin alone and in combination with **cholestyramine** in low dosage; a report of 2 years experiences]. HMG-CoA-Reduktase-Inhibitoren bei familiarer **Hypercholesterinamie**. Therapie mit Simvastatin allein und in Kombination mit Colestyramin in

niedriger Dosierung; ein Zwei-Jahres-Erfahrungsbericht.
AU Geisel J; Oette K; Burrichter H
CS Institut fur Klinische Chemie, Universitat Koln.
SO FORTSCHRITTE DER MEDIZIN, **(1990 Feb 10)** 108 (4) 71-2, 75-6.
Journal code: F62; 2984763R. ISSN: 0015-8178.
CY GERMANY, EAST: German Democratic Republic
DT Journal; Article; (JOURNAL ARTICLE)
LA German
FS Priority Journals
EM 199004
ED Entered STN: 19900601
Last Updated on STN: 19980206
Entered Medline: 19900425
AB We have studied the effect of simvastatin, an inhibitor of the rate-limiting enzyme in **cholesterol** biosynthesis, alone and in combination with **cholestyramine** in 48 patients. Simvastatin 40 mg decreased total serum **cholesterol**, LDL **cholesterol** and apolipoprotein B by 35%, 40% and 35%, respectively, while HDL **cholesterol** and apolipoprotein A-I increased by 10% (p less than 0.01) and 7% (p less than 0.05), respectively. The addition of 8 g **cholestyramine** caused a further decrease in total **cholesterol** and LDL **cholesterol** to a total of 42% and 49%, respectively. Eighteen of the 48 patients have now been under combined treatment for 2 years. The initial high decreases in total **cholesterol** and LDL **cholesterol** were stabilized for the whole period. Some patients developed gastrointestinal complaints, which made necessary a reduction of simvastatin in two cases. Biochemical side effects (e.g. increases in CK and transaminases) were not observed.
CT Check Tags: Female; Human; Male
Adult
***Anticholesteremic Agents: TU, therapeutic use**
***Cholestyramine: TU, therapeutic use**
Drug Therapy, Combination
*Hydroxymethylglutaryl CoA Reductases: AI, antagonists & inhibitors
***Hypercholesterolemia, Familial: DT, drug therapy**
***Lovastatin: AA, analogs & derivatives**
Lovastatin: TU, therapeutic use
Middle Age
Simvastatin
RN **11041-12-6 (Cholestyramine); 75330-75-5 (Lovastatin);** 79902-63-9 (Simvastatin)
CN 0 (**Anticholesteremic** Agents); EC 1.1.1.88 (Hydroxymethylglutaryl CoA Reductases)

L173 ANSWER 41 OF 63 MEDLINE
AN 90184098 MEDLINE
DN 90184098 PubMed ID: 2178931
TI Efficacy and safety of simvastatin (alone or in association with **cholestyramine**). A 1-year study in 66 patients with type II hyperlipoproteinaemia.
AU Emmerich J; Aubert I; Bauduceau B; Dachet C; Chanu B; Erlich D; Gautier D; Jacotot B; Rouffy J
CS Unite de recherches sur les dyslipidemies et l'atherosclerose, INSERM U 32, Hopital Henri Mondor, Creteil, France.
SO EUROPEAN HEART JOURNAL, **(1990 Feb)** 11 (2) 149-55.
Journal code: EM8; 8006263. ISSN: 0195-668X.
CY ENGLAND: United Kingdom
DT (CLINICAL TRIAL)
(CONTROLLED CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199004
ED Entered STN: 19900601
Last Updated on STN: 19980206
Entered Medline: 19900424

AB The effects and safety of simvastatin, an inhibitor of 3-hydroxy-3-methylglutaryl coenzyme A reductase, were investigated alone or in association with **cholestyramine** in 66 patients with **hypercholesterolaemia**, in a 1-year study. In type IIa **hypercholesterolaemia** (41 patients), the association was more effective than simvastatin used alone in lowering total **cholesterol** (37% vs 29%) and LDL-**cholesterol** (45% vs 37%). In type IIb **hypercholesterolaemia** (23 patients), the association simvastatin-**cholestyramine** did not appear more effective than simvastatin used alone. The decrease of apoprotein B was parallel to the LDL-**cholesterol** decrease. Apoprotein A1 did not change significantly. The long-term safety of simvastatin was good. No lens opacity was noted. The most serious side-effect in our study was myolysis which occurred in two patients with a marked increase in creatine phosphokinase.

CT Check Tags: Female; Human; Male
Adult
Aged
***Anticholesteremic Agents: TU, therapeutic use**
Apoproteins: ME, metabolism
***Cholestyramine: TU, therapeutic use**
Clinical Trials
Drug Therapy, Combination
Hypercholesterolemia, Familial: BL, blood
***Hypercholesterolemia, Familial: DT, drug therapy**
Lipids: BL, blood
***Lovastatin: AA, analogs & derivatives**
Lovastatin: TU, therapeutic use
Middle Age
Simvastatin

RN **11041-12-6 (Cholestyramine); 75330-75-5 (Lovastatin);** 79902-63-9 (Simvastatin)

CN 0 (**Anticholesteremic** Agents); 0 (Apoproteins); 0 (Lipids)

L173 ANSWER 42 OF 63 MEDLINE
AN 90154260 MEDLINE
DN 90154260 PubMed ID: 2105981
TI Silent myocardial ischemia--classification and management.
AU Cohn P F
CS State University of New York, Stony Brook.
SO HOSPITAL PRACTICE (OFFICE EDITION), **(1990 Feb 28)** 25 (2A) 45-6, 48-50.
Journal code: HPO; 8404149. ISSN: 8750-2836.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199003
ED Entered STN: 19900601
Last Updated on STN: 19900601
Entered Medline: 19900322

AB As many as 10% of middle-aged men in the United States may have asymptomatic but active coronary artery disease. Additional patients have silent disease after a myocardial infarction or a combination of silent ischemia and angina. Silent and painful episodes have similar hemodynamic and electrical properties, and antianginal medications appear to have global anti-ischemic effects.

CT Check Tags: Case Report; Human; Male
Angina Pectoris: PP, physiopathology
Atenolol: AD, administration & dosage
Drug Therapy, Combination
Heart Function Tests
Hemodynamics
Hypercholesterolemia: DT, drug therapy
Hypercholesterolemia: PP, physiopathology
Lovastatin: AD, administration & dosage

Middle Age
*Myocardial Infarction: DI, diagnosis
Myocardial Infarction: PP, physiopathology
Nifedipine: AD, administration & dosage
Risk Factors
RN 21829-25-4 (Nifedipine); 29122-68-7 (Atenolol); **75330-75-5 (Lovastatin)**

L173 ANSWER 43 OF 63 MEDLINE
AN 90060179 MEDLINE
DN 90060179 PubMed ID: 2511025
TI **Lovastatin** reduces postprandial lipoprotein levels in **hypercholesterolaemic** patients with mild hypertriglyceridaemia.
AU Weintraub M S; Eisenberg S; Breslow J L
CS Laboratory of Biochemical Genetics and Metabolism, Rockefeller University, New York 10021.
NC HL32435 (NHLBI)
HL33714 (NHLBI)
HL36461 (NHLBI)
+
SO EUROPEAN JOURNAL OF CLINICAL INVESTIGATION, **(1989 Oct)** 19 (5) 480-5.
Journal code: EN3; 0245331. ISSN: 0014-2972.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199001
ED Entered STN: 19900328
Last Updated on STN: 19970203
Entered Medline: 19900110
AB Drugs that inhibit **cholesterol** synthesis have recently been released for lowering LDL-**cholesterol** levels. The current study examines the effect of one of these drugs, **lovastatin**, alone and in combination with **cholestyramine** on postprandial fat metabolism in five patients with severely elevated LDL-**cholesterol** and normal triglyceride levels (less than 1.8 mmol l-1) and in five patients with similarly elevated LDL-**cholesterol** and mildly elevated triglyceride levels (1.8 to 2.7 mmol l-1). In the group of patients with normal triglyceride levels, neither **lovastatin** alone nor in combination with **cholestyramine** had any effect on postprandial lipoprotein levels, while profoundly decreasing LDL-**cholesterol** levels. This provides evidence that LDL and postprandial lipoproteins are cleared by different mechanisms. In the group of five patients with mildly elevated triglyceride levels, in addition to LDL-**cholesterol** lowering, **lovastatin** significantly lowered VLDL-**cholesterol**, fasting triglyceride and postprandial lipoprotein levels. Thus in patients with mild hypertriglyceridaemia, **lovastatin** may have another favourable effect on the lipoprotein system in addition to LDL-**cholesterol** lowering.
CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Adult
Aged
Cholestyramine: AD, administration & dosage
Cholestyramine: TU, therapeutic use
Drug Therapy, Combination
Hypercholesterolemia: BL, blood
Hypercholesterolemia: CO, complications
***Hypercholesterolemia: DT, drug therapy**
Hypertriglyceridemia: BL, blood
Hypertriglyceridemia: CO, complications
***Hypertriglyceridemia: DT, drug therapy**
*Lipoproteins: BL, blood
Lipoproteins, LDL Cholesterol: BL, blood

Lipoproteins, VLDL Cholesterol: BL, blood
Lovastatin: AD, administration & dosage
***Lovastatin: TU, therapeutic use**
Middle Age
Triglycerides: BL, blood
RN **11041-12-6 (Cholestyramine); 75330-75-5 (Lovastatin)**
CN 0 (Lipoproteins); 0 (Lipoproteins, LDL **Cholesterol**); 0 (Lipoproteins, VLDL **Cholesterol**); 0 (Triglycerides)

L173 ANSWER 44 OF 63 MEDLINE
AN 90039107 MEDLINE
DN 90039107 PubMed ID: 2681508
TI Simvastatin and **cholestyramine** in the long-term treatment of **hypercholesterolaemia.**
AU Ytre-Arne K; Nordoy A
CS Department of Medicine, Regionsykehuset i Tromso, Norway.
SO JOURNAL OF INTERNAL MEDICINE, **(1989 Nov)** 226 (5) 285-90.
Journal code: I2G; 8904841. ISSN: 0954-6820.
CY ENGLAND: United Kingdom
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LA English
FS Priority Journals
EM 198912
ED Entered STN: 19900328
Last Updated on STN: 19980206
Entered Medline: 19891221
AB After 6 weeks on a lipid-lowering diet, 20 outpatients with type II hyperlipoproteinaemia (18 type IIa) were randomized to treatment with **cholestyramine** 12 g b.i.d. (5 patients) or simvastatin (a new HMG-CoA reductase inhibitor) 40 mg q.p.m. (15 patients) for 12 weeks. From week 13 to week 20 nine patients in the simvastatin group and all patients in the **cholestyramine** group were treated with the combination of the two drugs. From week 21 to week 52 all patients were on monotherapy with simvastatin. Simvastatin treatment reduced low-density lipoprotein (LDL) **cholesterol** by 40% after 12 weeks, compared with 33% in the **cholestyramine** group. This difference was not significant. The total reductions of LDL-**cholesterol** on combination therapy were respectively 60% and 56% in each group. After 52 weeks LDL-**cholesterol** was still reduced by 36% (P less than 0.001) on monotherapy with simvastatin. Simvastatin also reduced triglycerides (TG) by 17% (P less than 0.05) and high-density lipoprotein (HDL) **cholesterol** was increased by 19% (P less than 0.01). No serious side effects were observed, and the new HMG-CoA reductase inhibitors may offer a new approach to the treatment of **hypercholesterolaemia.**
CT Check Tags: Comparative Study; Female; Human; Male
Adult
Aged
Alanine Transaminase: ME, metabolism
Anticholesteremic Agents: AE, adverse effects
***Anticholesteremic Agents: TU, therapeutic use**
***Cholestyramine: TU, therapeutic use**
Clinical Trials
Drug Therapy, Combination
Hypercholesterolemia: BL, blood
***Hypercholesterolemia: DT, drug therapy**
Lipids: BL, blood
Lovastatin: AE, adverse effects
***Lovastatin: AA, analogs & derivatives**
Lovastatin: TU, therapeutic use
Middle Age
Random Allocation
Simvastatin
Time Factors
RN **11041-12-6 (Cholestyramine); 75330-75-5 (Lovastatin);**

79902-63-9 (Simvastatin)
CN 0 (**Anticholesteremic** Agents); 0 (Lipids); EC 2.6.1.2 (Alanine Transaminase)

L173 ANSWER 45 OF 63 MEDLINE
AN 90038898 MEDLINE
DN 90038898 PubMed ID: 2809398
TI Contrasting effects of **lovastatin** and **cholestyramine** on low-density lipoprotein **cholesterol** and 24-hour urinary mevalonate excretion in patients with heterozygous familial **hypercholesterolemia**.
AU Pappu A S; Illingworth D R
CS Department of Medicine, Oregon Health Sciences University, Portland 97201.
NC HL28399 (NHLBI)
HL32271 (NHLBI)
HL37940 (NHLBI)
+
SO JOURNAL OF LABORATORY AND CLINICAL MEDICINE, **(1989 Nov)** 114 (5) 554-62.
Journal code: IVR; 0375375. ISSN: 0022-2143.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 198912
ED Entered STN: 19900328
Last Updated on STN: 19970203
Entered Medline: 19891215
AB To further validate the usefulness of quantitative measurements of urinary mevalonic acid excretion as an indicator of rates of **cholesterol** biosynthesis, we have determined the 24-hour urinary excretion of mevalonic acid in patients with heterozygous familial **hypercholesterolemia** treated with drugs that have opposing effects on **cholesterol** biosynthesis. In patients with familial **hypercholesterolemia** treated with the bile acid sequestrant **cholestyramine** (16 gms/day), urinary mevalonate excretion increased by 28%, whereas low-density lipoprotein **cholesterol** concentrations decreased by 21%. In patients with familial **hypercholesterolemia** treated with the 3-hydroxy 3-methyl glutaryl coenzyme A reductase inhibitor **lovastatin** (80 mg/day), concentrations of low-density lipoprotein **cholesterol** and the urinary excretion of mevalonate both decreased (by 40% and 34%, respectively). When **cholestyramine** was used in combination with **lovastatin**, low-density lipoprotein **cholesterol** levels decreased by an additional 14% as compared to monotherapy with **lovastatin**; urinary mevalonate excretion rose by (25%), but the magnitude of this increase was not statistically significant. We conclude that rates of excretion of urinary mevalonic acid (which may reflect rates of whole body **cholesterol** biosynthesis) in patients with FH decrease on therapy with **lovastatin** and increase in response to **cholestyramine** treatment. When used in combination, these drugs counteract each other's effects on **cholesterol** synthesis, but low-density lipoprotein **cholesterol** concentrations decrease further. Measurement of urinary mevalonate excretion affords a practical means of assessing the comparable effects of different dietary or pharmaceutical manipulations on **cholesterol** biosynthesis in human beings.
CT Check Tags: Female; Human; Male; Support, U.S. Gov't, P.H.S.
Adult
Cholestyramine: AD, administration & dosage
***Cholestyramine: TU, therapeutic use**
Drug Therapy, Combination
Heterozygote
***Hypercholesterolemia, Familial: DT, drug therapy**
Hypercholesterolemia, Familial: GE, genetics
Hypercholesterolemia, Familial: ME, metabolism

***Lipoproteins, LDL Cholesterol: BL, blood**
Lovastatin: AD, administration & dosage
***Lovastatin: TU, therapeutic use**
*Mevalonic Acid: UR, urine
RN **11041-12-6 (Cholestyramine)**; 150-97-0 (Mevalonic Acid); **75330-75-5 (Lovastatin)**
CN 0 (Lipoproteins, LDL **Cholesterol**)

L173 ANSWER 46 OF 63 MEDLINE
AN 90023567 MEDLINE
DN 90023567 PubMed ID: 2552800
TI Normalization of LDL receptor function by lymphocytes of patients with heterozygous familial **hypercholesterolemia** after treatment with plasma **cholesterol** lowering agents.
AU Cuthbert J A; East C A; Lipsky P E
CS Department of Internal Medicine, University of Texas Southwestern Medical Center, Dallas.
NC AI-17653 (NIAID)
HL-29252 (NHLBI)
MO1-RR00633 (NCRR)
+
SO AMERICAN JOURNAL OF THE MEDICAL SCIENCES, **(1989 Sep)** 298 (3) 152-60.
Journal code: 3L2; 0370506. ISSN: 0002-9629.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 198910
ED Entered STN: 19900328
Last Updated on STN: 19970203
Entered Medline: 19891031
AB Low density lipoprotein (LDL)-dependent growth of mitogen-activated lymphocytes, inhibited in their capacity to synthesize **cholesterol** endogenously, can be used as an assay of functional receptors for LDL. Using this technique, abnormalities can be detected in circulating lymphocytes obtained from patients with familial **hypercholesterolemia** (FH). Functional lymphocyte LDL receptor activity was decreased in patients with heterozygous FH. Following treatment with the specific inhibitor of **cholesterol** synthesis, **lovastatin**, alone or in combination with a bile acid-binding resin, there was increased expression of functional lymphocyte LDL receptors in five of nine patients. Plasma LDL **cholesterol** levels decreased in all nine patients. Three other patients who were only studied while receiving therapy also manifested increased expression of functional lymphocyte LDL receptors. The degree of improvement in plasma LDL **cholesterol** did not predict the effect on lymphocyte LDL receptor function. Longitudinal studies indicated that an increase in functional LDL receptor activity could be observed with 4 weeks of therapy and persisted for at least 18 months on continuous treatment. These results provide direct evidence that therapy with **lovastatin** and a bile acid-binding resin can lead to increased expression of functional LDL receptors by lymphocytes in the majority (eight of 12) of patients with heterozygous FH.
CT Check Tags: Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
***Anticholesteremic Agents: TU, therapeutic use**
Cholestyramine: TU, therapeutic use
Colestipol: TU, therapeutic use
Drug Combinations
*Heterozygote
***Hypercholesterolemia, Familial: DT, drug therapy**
Hypercholesterolemia, Familial: GE, genetics
Hypercholesterolemia, Familial: PP, physiopathology
Lipoproteins
***Lipoproteins, LDL: ME, metabolism**
Lovastatin: TU, therapeutic use

*Lymphocytes: PH, physiology
*Receptors, Cell Surface: PH, physiology
Receptors, Lipoprotein
Reference Values
RN **11041-12-6 (Cholestyramine)**; 50925-79-6 (Colestipol); **75330-75-5 (Lovastatin)**
CN 0 (**Anticholesteremic** Agents); 0 (Drug Combinations); 0 (Lipoproteins); 0 (Lipoproteins, LDL); 0 (Receptors, Cell Surface); 0 (Receptors, Lipoprotein)

L173 ANSWER 47 OF 63 MEDLINE
AN 90023562 MEDLINE
DN 90023562 PubMed ID: 2801750
TI Simvastatin: the clinical profile.
AU Walker J F
CS Merck Sharp & Dohme Research Laboratories, Rahway, New Jersey 07065.
SO AMERICAN JOURNAL OF MEDICINE, **(1989 Oct 16)** 87 (4A) 44S-46S.
Journal code: 3JU; 0267200. ISSN: 0002-9343.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 198911
ED Entered STN: 19900328
Last Updated on STN: 19980206
Entered Medline: 19891120
AB Simvastatin is the second in the class of compounds known as hydroxy-methylglutaryl-coenzyme A reductase inhibitors to be extensively studied in humans. The drug has now been given to over 1,800 patients with primary **hypercholesterolemia** for periods of up to two years. In the range of dosage from 10 to 40 mg once daily, therapy is associated with reductions of up to 30 percent in total **cholesterol** and 40 percent in low-density lipoprotein **cholesterol** levels, as well as with increases of approximately 10 percent in high-density lipoprotein **cholesterol** levels. The most common clinical adverse experiences are mild gastrointestinal effects and headache, which seldom require discontinuation of therapy. Elevations of creatine kinase (skeletal muscle isoenzyme) levels to more than three times the upper limit of the normal range have been seen in about 3 percent of patients, but also have seldom required discontinuation of therapy. Conversely, elevations of hepatic transaminase levels to more than three times the upper limit of the laboratory normal range have been seen in about 1.5 percent of patients and have caused discontinuation of therapy in 0.6 percent of patients treated. Simvastatin appears to be an effective and well-tolerated agent for the treatment of primary **hypercholesterolemia** and, as further study confirms long-term safety and efficacy, it should become a useful addition to the therapeutic armamentarium.
CT Check Tags: Female; Human; Male
Aged
Creatine Kinase: BL, blood
Drug Therapy, Combination
Eye: DE, drug effects
*Hydroxymethylglutaryl CoA Reductases: AI, antagonists & inhibitors
***Hypercholesterolemia: DT, drug therapy**
Hypercholesterolemia: EN, enzymology
***Hypercholesterolemia, Familial: DT, drug therapy**
Liver: DE, drug effects
Lovastatin: AE, adverse effects
***Lovastatin: AA, analogs & derivatives**
Lovastatin: PK, pharmacokinetics
Lovastatin: TU, therapeutic use
Middle Age
Simvastatin
Transaminases: BL, blood
RN **75330-75-5 (Lovastatin)**; 79902-63-9 (Simvastatin)
CN EC 1.1.1.88 (Hydroxymethylglutaryl CoA Reductases); EC 2.6.1.

(Transaminases); EC 2.7.3.2 (Creatine Kinase)

L173 ANSWER 48 OF 63 MEDLINE
AN 90023561 MEDLINE
DN 90023561 PubMed ID: 2679083
TI Efficacy and tolerability of simvastatin (MK-733).
AU Stalenhoef A F; Mol M J; Stuyt P M
CS Department of Internal Medicine, University Hospital Nijmegen, The Netherlands.
SO AMERICAN JOURNAL OF MEDICINE, **(1989 Oct 16)** 87 (4A) 39S-43S.
Ref: 16
Journal code: 3JU; 0267200. ISSN: 0002-9343.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 198911
ED Entered STN: 19900328
Last Updated on STN: 19980206
Entered Medline: 19891120
AB The efficacy of simvastatin, a new inhibitor of **cholesterol** biosynthesis, was studied in patients with familial **hypercholesterolemia**. A mean reduction in low-density lipoprotein **cholesterol** of 38 percent was observed after eight weeks of treatment with 20 mg of simvastatin; a 42 percent reduction was seen after the next 16 weeks with 40 mg. There was no difference in response whether the drug was taken in one or two doses. In another study, simvastatin (40 mg per day) was compared with **cholestyramine** (8 to 16 g per day). After 12 weeks, low-density lipoprotein **cholesterol** was reduced 43 percent by simvastatin and 29 percent by **cholestyramine** . Combination therapy caused a reduction in low-density lipoprotein **cholesterol** of 54 percent. Simvastatin appeared also to be a potent hypolipidemic drug in 10 patients with familial dysbetalipoproteinemia. The drug was well tolerated. Adverse effects were primarily composed of increases in serum transaminases and creatine phosphokinase. No effects of simvastatin on the production of steroid hormones were observed.
CT Check Tags: Female; Human; Male
Adrenal Cortex: DE, drug effects
Adult
Aged
***Anticholesteremic Agents: TU, therapeutic use**
Cholestyramine: TU, therapeutic use
Drug Therapy, Combination
***Hypercholesterolemia, Familial: DT, drug therapy**
Lipoproteins, LDL Cholesterol: BL, blood
Lovastatin: AE, adverse effects
***Lovastatin: AA, analogs & derivatives**
Lovastatin: TU, therapeutic use
Middle Age
Simvastatin
RN **11041-12-6 (Cholestyramine); 75330-75-5 (Lovastatin);** 79902-63-9 (Simvastatin)
CN 0 (**Anticholesteremic** Agents); 0 (Lipoproteins, LDL **Cholesterol**)

L173 ANSWER 49 OF 63 MEDLINE
AN 89391895 MEDLINE
DN 89391895 PubMed ID: 2675812
TI Simvastatin (MK 733): an effective treatment for **hypercholesterolemia**.
AU Lintott C J; Scott R S; Nye E R; Robertson M C; Sutherland W H
CS Department of Medicine, Princess Margaret Hospital, Christchurch, New Zealand.

SO AUSTRALIAN AND NEW ZEALAND JOURNAL OF MEDICINE, **(1989 Aug)** 19 (4) 317-20.
Journal code: 9H9; 1264322. ISSN: 0004-8291.
CY Australia
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LA English
FS Priority Journals
EM 198910
ED Entered STN: 19900309
Last Updated on STN: 19980206
Entered Medline: 19891019
AB This study describes the efficacy of the drug simvastatin. It is likely to be the first HMG CoA reductase inhibitor in Australia and New Zealand available for the treatment of hyperlipidemia. Twenty-four patients, 12 men and 12 women with primary **hypercholesterolemia** were randomly allocated to treatment by **cholestyramine** (eight patients) or to simvastatin (16 patients) for a 12-week period. With simvastatin, total **cholesterol** levels decreased by 37.5% from a baseline mean of 10.33 mmol/L to 6.4 mmol/L after 12 weeks. Low density lipoprotein (LDL) **cholesterol** concentration decreased by 48.2% from 8.40 mmol/L to 4.39 mmol/L. These effects were better than observed for **cholestyramine** alone where **cholesterol** and LDL-**cholesterol** reductions were 24.9% and 33.1% respectively. Thirteen patients, however, did not achieve target LDL levels of 3.62 mmol/L, or below, and therefore were treated with a combination of **cholestyramine** and simvastatin, resulting in a decrease of total **cholesterol** and LDL-**cholesterol** by 45.5% and 53.5% of baseline values studied over an eight-week period. No major clinical side-effects were encountered. One patient appeared to have had a change in colour vision at the end of the study at 20 weeks, without loss of visual acuity.
CT Check Tags: Female; Human; Male
Adult
Aged
Anticholesteremic Agents: AD, administration & dosage
***Anticholesteremic Agents: TU, therapeutic use**
Cholesterol: BL, blood
Cholestyramine: AD, administration & dosage
Cholestyramine: TU, therapeutic use
Clinical Trials
Drug Therapy, Combination
Hypercholesterolemia: BL, blood
***Hypercholesterolemia: DT, drug therapy**
Lipoproteins, LDL Cholesterol: BL, blood
Lovastatin: AD, administration & dosage
***Lovastatin: AA, analogs & derivatives**
Lovastatin: TU, therapeutic use
Middle Age
Random Allocation
Simvastatin
RN **11041-12-6 (Cholestyramine); 57-88-5 (Cholesterol); 75330-75-5 (Lovastatin);** 79902-63-9 (Simvastatin)
CN 0 (**Anticholesteremic** Agents); 0 (Lipoproteins, LDL **Cholesterol**)

L173 ANSWER 50 OF 63 MEDLINE
AN 89182068 MEDLINE
DN 89182068 PubMed ID: 2927555
TI [Efficacy and safety of simvastatin, a new **cholesterol**-lowering drug].
Effectiviteit en veiligheid van simvastatine, een nieuw **cholesterolverlagend** geneesmiddel.
AU Mol M J; Stuyt P M; Stalenhoef A F
SO NEDERLANDS TIJDSCHRIFT VOOR GENEESKUNDE, **(1989 Feb 18)** 133 (7)

362-6.
Journal code: NUK; 0400770. ISSN: 0028-2162.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA Dutch
FS Priority Journals
EM 198905
ED Entered STN: 19900306
Last Updated on STN: 19980206
Entered Medline: 19890511
AB The effects of simvastatin, an inhibitor of **cholesterol** synthesis, was studied in 50 patients with **hypercholesterolaemia**. In the first study, 24 patients with serum **cholesterol** levels of 10.74 +/- 1.59 mmol/l were treated with simvastatin 40 mg daily for 6 months. Serum **cholesterol** levels decreased within 4 to 8 weeks to stable values 30 to 36% below the basal value. Serum triglycerides decreased by 16 to 28% and high density lipoprotein (HDL) **cholesterol** increased by 6 to 11% on average. In the second study, 26 patients with serum **cholesterol** levels of 12.35 +/- 2.05 mmol/l were treated with simvastatin 40 mg daily as monotherapy or combined with a bile acid binding resin for 2 years. **Cholesterol** levels decreased to values which remained stable throughout the entire study period; after 2 years the decrease amounted to 43%. Compared with monotherapy, combination with a bile acid binding resin yielded a further 12% decrease of **cholesterol**. In the entire group, triglycerides decreased by 16% and HDL **cholesterol** increased by 9% on the average. Side effects were limited to slight increases in alanine aminotransferase and creatine phosphokinase occurring in some patients. Simvastatin appears to be an important asset in the treatment of **hypercholesterolaemia.**
CT Check Tags: Female; Human; Male
***Anticholesteremic Agents: TU, therapeutic use**
Cholesterol: BL, blood
Cholestyramine: AD, administration & dosage
Drug Therapy, Combination
*Hydroxymethylglutaryl CoA Reductases: AI, antagonists & inhibitors
***Hypercholesterolemia: DT, drug therapy**
Lovastatin: AD, administration & dosage
Lovastatin: AE, adverse effects
***Lovastatin: AA, analogs & derivatives**
Lovastatin: TU, therapeutic use
Middle Age
Simvastatin
RN **11041-12-6 (Cholestyramine); 57-88-5 (Cholesterol); 75330-75-5 (Lovastatin);** 79902-63-9 (Simvastatin)
CN 0 (**Anticholesteremic** Agents); EC 1.1.1.88 (Hydroxymethylglutaryl CoA Reductases)

L173 ANSWER 51 OF 63 MEDLINE
AN 89136172 MEDLINE
DN 89136172 PubMed ID: 2645064
TI Influence of **lovastatin** plus gemfibrozil on plasma lipids and lipoproteins in patients with heterozygous familial **hypercholesterolemia.**
AU Illingworth D R; Bacon S
CS Department of Medicine, Oregon Health Sciences University, Portland 97201.
NC HL-32271 (NHLBI)
HL-37940 (NHLBI)
RR334 (NCRR)
SO CIRCULATION, **(1989 Mar)** 79 (3) 590-6.
Journal code: DAW; 0147763. ISSN: 0009-7322.
CY United States
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals

EM 198904
ED Entered STN: 19900306
Last Updated on STN: 19970203
Entered Medline: 19890406
AB We investigated the **hypocholesterolemic** effects of **lovastatin** alone and in combination with gemfibrozil on plasma lipids and lipoproteins in 12 adult patients with well-characterized heterozygous familial **hypercholesterolemia**. Plasma concentrations of low density lipoprotein (LDL) **cholesterol** decreased from 321 +/- 14 mg/dl on diet only to 207 +/- 8 mg/dl (-35.5%) on single-drug therapy with **lovastatin** at a dose of 40 mg twice daily, whereas triglyceride concentrations fell by 27.6% (from 145 +/- 20 to 105 +/- 20 mg/dl). Subsequent addition of gemfibrozil at a dose of 600 mg twice daily resulted in a nonsignificant further reduction in LDL **cholesterol** to 194 +/- 7 mg/dl (-39.6% change from baseline), whereas triglycerides decreased to 80 mg/dl (-44.8%, p less than 0.05 vs. single-drug therapy with **lovastatin**). Plasma concentrations of high density lipoprotein (HDL) increased slightly during **lovastatin** and combined drug therapy (from 45 +/- 4 mg/dl at baseline to 46 +/- 4 mg/dl on **lovastatin** to 48 +/- 4 mg/dl on **lovastatin** plus gemfibrozil). The response to combination drug therapy in individual patients was heterogeneous and clinically significant decreases in LDL **cholesterol** concentrations were noted in two of the 12 patients, whereas in three patients LDL **cholesterol** concentrations increased on the combined drug regimen. One patient developed an asymptomatic increase in creatine kinase on monotherapy with **lovastatin** and a more pronounced and symptomatic increase during combination drug therapy with **lovastatin** plus gemfibrozil.(ABSTRACT TRUNCATED AT 250 WORDS)
CT Check Tags: Comparative Study; Female; Human; Male; Support, U.S. Gov't, P.H.S.
Adult
Clinical Trials
Drug Therapy, Combination
*Gemfibrozil: TU, therapeutic use
Heterozygote
Hypercholesterolemia, Familial: BL, blood
***Hypercholesterolemia, Familial: DT, drug therapy**
Lipoproteins, HDL Cholesterol: BL, blood
Lipoproteins, LDL Cholesterol: BL, blood
***Lovastatin: TU, therapeutic use**
Middle Age
Triglycerides: BL, blood
RN 25812-30-0 (Gemfibrozil); **75330-75-5 (Lovastatin)**
CN 0 (Lipoproteins, HDL **Cholesterol**); 0 (Lipoproteins, LDL **Cholesterol**); 0 (Triglycerides)

L173 ANSWER 52 OF 63 MEDLINE
AN 89104816 MEDLINE
DN 89104816 PubMed ID: 2492189
TI Treatment of heterozygous familial **hypercholesterolemia** with lipid-lowering drugs.
AU Illingworth D R; Bacon S
CS Department of Medicine, Oregon Health Sciences University, Portland 97201.
NC HL28399 (NHLBI)
HL32271 (NHLBI)
HL37940 (NHLBI)
+
SO ARTERIOSCLEROSIS, **(1989 Jan-Feb)** 9 (1 Suppl) I121-34. Ref: 73
Journal code: 89S; 8401388. ISSN: 0276-5047.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals

EM 198902
ED Entered STN: 19900308
Last Updated on STN: 19980206
Entered Medline: 19890222
AB Patients with heterozygous familial **hypercholesterolemia** (FH) constitute a unique population at high risk for the premature development of coronary artery disease (CAD) and in whom long-term **hypocholesterolemic** therapy to reduce elevated levels of low density lipoprotein (LDL) **cholesterol** is most clearly indicated. Optimal therapy invariably requires diet regulation plus hypolipidemic drug therapy. When used as single agents, the bile-acid sequestrants, **cholestyramine** and colestipol, lower LDL **cholesterol** concentrations by 20% to 35% in compliant patients, whereas decreases of 20% to 30% can be achieved with nicotinic acid in doses of 3 to 6 g/day. Bezafibrate, fenofibrate, and ciprofibrate have also been shown to lower LDL **cholesterol** levels by 20% to 30%, and these drugs are more effective than gemfibrozil and clofibrate. Probucol, neomycin, and D-thyroxine reduce LDL **cholesterol** concentrations by 10% to 15% in single-drug use. Clinical trials with a new class of drugs that inhibit the rate-limiting enzyme in **cholesterol** biosynthesis, 3-hydroxy-3-methylglutaryl coenzyme A (HMG CoA) reductase, and that includes **lovastatin**, simvastatin, and pravastatin indicate that these drugs lower LDL **cholesterol** concentrations by 30% to 50% in patients with heterozygous FH. Combined drug therapy with a bile-acid sequestrant and nicotinic acid lowers LDL **cholesterol** by 40% to 55%, whereas fenofibrate, bezafibrate, or probucol plus a bile-acid sequestrant results in reductions varying from 25% to 50%. The combinations of an HMG CoA reductase inhibitor with either a bile-acid sequestrant or nicotinic acid appears to be the most promising, and these regimens reduce LDL **cholesterol** levels by 45% to 60%. With appropriate use, the currently available **hypocholesterolemic** drugs have the potential to markedly change the natural history of premature atherosclerosis that occurs in untreated patients with FH.
CT Check Tags: Human; Support, U.S. Gov't, P.H.S.
Butyrates: TU, therapeutic use
Cholestyramine: TU, therapeutic use
Colestipol: TU, therapeutic use
Drug Therapy, Combination
Gemfibrozil: TU, therapeutic use
Heptanoic Acids: TU, therapeutic use
Heterozygote
Hydroxymethylglutaryl CoA Reductases: AI, antagonists & inhibitors
***Hypercholesterolemia, Familial: DT, drug therapy**
Lovastatin: AA, analogs & derivatives
Lovastatin: TU, therapeutic use
Naphthalenes: TU, therapeutic use
Neomycin: TU, therapeutic use
Niacin: TU, therapeutic use
Pravastatin
Probucol: TU, therapeutic use
Simvastatin
Thyroxine: TU, therapeutic use
RN **11041-12-6 (Cholestyramine)**; 1404-04-2 (Neomycin); 23288-49-5 (Probucol); 25812-30-0 (Gemfibrozil); 50925-79-6 (Colestipol); 59-67-6 (Niacin); 7488-70-2 (Thyroxine); **75330-75-5 (Lovastatin)**; 79902-63-9 (Simvastatin); 81093-37-0 (Pravastatin)
CN 0 (Butyrates); 0 (Heptanoic Acids); 0 (Naphthalenes); EC 1.1.1.88 (Hydroxymethylglutaryl CoA Reductases)

L173 ANSWER 53 OF 63 MEDLINE
AN 89090090 MEDLINE
DN 89090090 PubMed ID: 2642754
TI Intensive combination drug therapy of familial **hypercholesterolemia** with **lovastatin**, probucol, and colestipol hydrochloride.
AU Witztum J L; Simmons D; Steinberg D; Beltz W F; Weinreb R; Young S G;

Lester P; Kelly N; Juliano J
CS Department of Medicine, University of California, San Diego, La Jolla 92093-0613.
NC HL-14197 (NHLBI)
PHS-RR-00827 (NCRR)
SO CIRCULATION, **(1989 Jan)** 79 (1) 16-28.
Journal code: DAW; 0147763. ISSN: 0009-7322.
CY United States
DT (CLINICAL TRIAL)
(CONTROLLED CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 198902
ED Entered STN: 19900308
Last Updated on STN: 19970203
Entered Medline: 19890222
AB Patients with familial **hypercholesterolemia** (FH) have had a life-long sustained elevation of low-density lipoprotein (LDL) **cholesterol** levels. Consequently, there is a need to maximally lower their elevated levels, and this usually requires lowering LDL levels more than 50%. Because no single hypolipidemic drug will consistently produce such degrees of lowering, combination drug therapy with two or even three agents is required to produce the desired degree of **cholesterol** lowering. A prospective trial was designed to determine if combination therapy using three hypolipidemic agents could effectively lower LDL levels in 17 severely affected FH subjects. Colestipol hydrochloride (10 g b.i.d.), probucol (500 mg b.i.d.), and **lovastatin** (20 or 40 mg b.i.d.) were given to each patient, in varying combinations, over a 25-month period. **Lovastatin** (40 mg/day) uniformly lowered LDL levels 36%. Probucol lowered LDL only 14% and in a variable manner. The combination of **lovastatin** and probucol lowered LDL no better than **lovastatin** alone. **Lovastatin** plus colestipol lowered LDL 52%; probucol added as a third agent produced no further lowering. **Lovastatin** (80 mg/day) plus colestipol lowered LDL 56%. **Lovastatin** increased high-density lipoprotein (HDL) **cholesterol** levels 6%, whereas probucol decreased HDL 29%. In all patients there was an effective lowering of LDL levels, ranging from 40% to 70%. Thus, **lovastatin** plus colestipol is an effective hypolipidemic regimen for producing marked decreases in LDL levels in FH subjects. The addition of probucol as a third hypolipidemic agent adds little to the therapeutic regimen as measured by lowering of LDL levels.
CT Check Tags: Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Cholesterol: BL, blood
Clinical Trials
Colestipol: AE, adverse effects
*Colestipol: TU, therapeutic use
Drug Interactions
Drug Therapy, Combination
Hypercholesterolemia, Familial: BL, blood
***Hypercholesterolemia, Familial: DT, drug therapy**
Lipoproteins, HDL: BL, blood
Lipoproteins, LDL: BL, blood
Lovastatin: AE, adverse effects
***Lovastatin: TU, therapeutic use**
*Phenols: TU, therapeutic use
*Polyamines: TU, therapeutic use
Probucol: AE, adverse effects
***Probucol: TU, therapeutic use**
Prospective Studies
Triglycerides: BL, blood
Xanthomatosis: BL, blood
RN 23288-49-5 (Probucol); 50925-79-6 (Colestipol); **57-88-5 (Cholesterol); 75330-75-5 (Lovastatin)**
CN 0 (Lipoproteins, HDL); 0 (Lipoproteins, LDL); 0 (Phenols); 0 (Polyamines);

0 (Triglycerides)

L173 ANSWER 54 OF 63 MEDLINE
AN 89050411 MEDLINE
DN 89050411 PubMed ID: 3056429
TI Effects of **lovastatin** alone and in combination with **cholestyramine** on serum lipids and apolipoproteins in heterozygotes for familial **hypercholesterolemia**.
AU Leren T P; Hjermann I; Berg K; Leren P; Foss O P; Viksmoen L
CS Medical Out-Patient Clinic, Ulleval Hospital, Oslo, Norway.
SO ATHEROSCLEROSIS, **(1988 Oct)** 73 (2-3) 135-41.
Journal code: 95X; 0242543. ISSN: 0021-9150.
CY Netherlands
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198812
ED Entered STN: 19900308
Last Updated on STN: 19900308
Entered Medline: 19881207
AB We have studied the effect of **lovastatin**, an inhibitor of the rate-limiting enzyme in **cholesterol** biosynthesis (3-hydroxy-3-methylglutaryl coenzyme A reductase), alone and in combination with the bile acid sequestrant **cholestyramine** on lipid parameters in 30 heterozygous patients with familial **hypercholesterolemia** (FH) during a 20-week open trial. **Lovastatin** 40 mg bid (twice daily) decreased significantly total serum **cholesterol**, low density lipoprotein (LDL)-**cholesterol**, triglycerides and apolipoprotein B by 36%, 45%, 29% and 11%, respectively, while high density lipoprotein (HDL)-**cholesterol** and apolipoprotein A-I were increased significantly by 16% and 37%, respectively. These data are consistent with a reduction in both the number of LDL particles and in their **cholesterol** content. Addition of **cholestyramine** 4 g bid caused a significant further decrease in total serum **cholesterol** and LDL-**cholesterol** to a total of 43% and 61%, respectively. The addition of 4 g bid or 8 g bid of **cholestyramine** caused only minor changes in the other lipid parameters. No effect was found by these drugs on Lp(a) lipoprotein level. We conclude that **lovastatin** alone or in combination with a small dose of **cholestyramine** normalizes the lipid profile in most FH heterozygotes.
CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't
Adult
*Apolipoproteins: BL, blood
***Cholestyramine: AD, administration & dosage**
Cholestyramine: AE, adverse effects
Cholestyramine: TU, therapeutic use
Clinical Trials
Drug Therapy, Combination
Heterozygote
Hypercholesterolemia, Familial: BL, blood
***Hypercholesterolemia, Familial: DT, drug therapy**
Hypercholesterolemia, Familial: GE, genetics
*Lipids: BL, blood
***Lovastatin: AD, administration & dosage**
Lovastatin: AE, adverse effects
Lovastatin: TU, therapeutic use
Middle Age
RN **11041-12-6 (Cholestyramine); 75330-75-5 (Lovastatin)**
CN 0 (Apolipoproteins); 0 (Lipids)

L173 ANSWER 55 OF 63 MEDLINE
AN 88239259 MEDLINE
DN 88239259 PubMed ID: 3288029
TI Combination drug therapy for familial combined hyperlipidemia.

AU East C; Bilheimer D W; Grundy S M
CS University of Texas Southwestern Medical Center, Dallas.
NC AM 07307 (NIADDK)
HL 29252 (NHLBI)
MO1-RR00633 (NCRR)
SO ANNALS OF INTERNAL MEDICINE, **(1988 Jul 1)** 109 (1) 25-32.
Journal code: 5A6; 0372351. ISSN: 0003-4819.
CY United States
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 198807
ED Entered STN: 19900308
Last Updated on STN: 19970203
Entered Medline: 19880711
AB STUDY OBJECTIVE: To compare the efficacy of gemfibrozil and colestipol with gemfibrozil and **lovastatin** in patients with familial combined hyperlipidemia. DESIGN: A prospective, randomized trial. SETTING: An outpatient clinical research center in a tertiary care center. PATIENTS: Seventeen patients with familial combined hyperlipidemia documented by studies of first-degree relatives; nine patients with type 2b hyperlipoproteinemia, and eight patients with type 4 hyperlipoproteinemia. INTERVENTIONS: Baseline lipid, lipoprotein, and apolipoprotein levels were obtained during control periods on diet alone and on gemfibrozil therapy. Patients then received gemfibrozil and colestipol or gemfibrozil and **lovastatin** in a randomized order. MEASUREMENTS AND MAIN RESULTS: In patients with type 2b hyperlipoproteinemia, gemfibrozil alone significantly reduced total **cholesterol** by 11%, and low density lipoprotein (LDL)-apolipoprotein B by 18%, did not change LDL-**cholesterol**, and raised high density lipoprotein (HDL)-**cholesterol** levels by 26%. Addition of either colestipol or **lovastatin** reduced LDL-**cholesterol** levels by 17% and 25%, respectively, compared to gemfibrozil alone. However, colestipol mitigated the HDL-**cholesterol** raising effect of gemfibrozil and did not further reduce LDL-apolipoprotein B levels. In contrast, addition of **lovastatin** caused an additional reduction of LDL-apolipoprotein B 19% compared with gemfibrozil alone. In patients with type 4 hyperlipoproteinemia, gemfibrozil alone reduced triglycerides by 40%, raised HDL-**cholesterol** by 26%, and increased LDL-**cholesterol** levels by 29%. The addition of either colestipol or **lovastatin** reduced LDL-**cholesterol** levels by 34% and 33%, respectively (compared with gemfibrozil alone), but greater reductions of LDL-apolipoprotein B (30% with **lovastatin** compared with 15% with colestipol, compared with gemfibrozil alone), and increases in HDL-**cholesterol** levels (8% increase with **lovastatin** compared with 10% decrease with colestipol, compared to gemfibrozil alone) were seen with the **lovastatin** combination. CONCLUSIONS: Although gemfibrozil with either colestipol or **lovastatin** favorably altered lipoprotein levels in patients with hypertriglyceridemia and familial combined hyperlipidemia, the combination of gemfibrozil and **lovastatin** appeared superior overall.
CT Check Tags: Comparative Study; Female; Human; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Adult
*Antilipemic Agents: TU, therapeutic use
Cholelithiasis: DI, diagnosis
*Colestipol: TU, therapeutic use
Drug Therapy, Combination
Gemfibrozil
Hypercholesterolemia, Familial: DT, drug therapy
Hyperlipidemia, Familial Combined: BL, blood
***Hyperlipidemia, Familial Combined: DT, drug therapy**
Hyperlipoproteinemia Type IV: DT, drug therapy

***Lovastatin: TU, therapeutic use**
Middle Age
*Pentanoic Acids: TU, therapeutic use
*Polyamines: TU, therapeutic use
Random Allocation
Ultrasonography
*Valerates: TU, therapeutic use
RN 25812-30-0 (Gemfibrozil); 50925-79-6 (Colestipol); **75330-75-5 (Lovastatin)**
CN 0 (Antilipemic Agents); 0 (Pentanoic Acids); 0 (Polyamines); 0 (Valerates)

L173 ANSWER 56 OF 63 MEDLINE
AN 88022223 MEDLINE
DN 88022223 PubMed ID: 3662275
TI Complementarity of colestipol, niacin, and **lovastatin** in treatment of severe familial **hypercholesterolemia**.
AU Malloy M J; Kane J P; Kunitake S T; Tun P
CS Cardiovascular Research Institute, University of California, San Francisco.
NC HL 14237 (NHLBI)
HL 31210 (NHLBI)
RR-79 (NCRR)
+
SO ANNALS OF INTERNAL MEDICINE, **(1987 Nov)** 107 (5) 616-23.
Journal code: 5A6; 0372351. ISSN: 0003-4819.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 198711
ED Entered STN: 19900305
Last Updated on STN: 19970203
Entered Medline: 19871120
AB OBJECTIVE: To compare the effectiveness of the ternary-drug combination of colestipol, niacin, and **lovastatin** with binary combinations of those drugs in treating patients with familial **hypercholesterolemia**. DESIGN: An open sequential study of serum lipoprotein responses in patients receiving diet alone (mean duration, 4 months); colestipol and niacin with diet (mean duration, 9 months); and colestipol, niacin, and **lovastatin** with diet (mean duration, 15 months). SETTING: Metabolic ward and lipid clinic of a university medical center. PATIENTS: Twenty-two patients with clinical characteristics of familial **hypercholesterolemia** (low-density-lipoprotein **cholesterol**, greater than 8.48 mmol/L; 21 of 22 with tendon xanthomas). INTERVENTIONS: Diet: less than 200 mg/d of **cholesterol** and less than 8% of total calories from saturated fat; colestipol, 30 g/d; **lovastatin**, 40 to 60 mg/d; and niacin, 1.5 to 7.5 g/d. MEASUREMENTS AND MAIN RESULTS: Mean total serum **cholesterol** and low-density-lipoprotein **cholesterol** levels of 4.86 +/- 0.62 mmol/L (188 +/- 24 mg/dL SD) and 2.89 +/- 0.54 mmol/L (112 +/- 21 mg/dL SD), respectively, were significantly lower during ternary-drug treatment than during colestipol-niacin treatment (p less than 0.003) or during treatment in which other possible binary combinations were given. The **cholesterol** content of very low-density-lipoproteins was lower and high-density-lipoprotein **cholesterol** levels higher during this phase than during the colestipol-niacin phase. CONCLUSIONS: Colestipol, **lovastatin**, and niacin are mutually complementary in treating **hypercholesterolemia**. This regimen produces reductions in serum **cholesterol** levels similar to those associated with regression of atheromatous plaques in animal studies.
CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Adult
Aged
Apolipoproteins B: BL, blood
Cholesterol: BL, blood

*Colestipol: AD, administration & dosage
Drug Therapy, Combination
Heterozygote
Homozygote
***Hypercholesterolemia, Familial: DT, drug therapy**
Hypercholesterolemia, Familial: GE, genetics
Lipoproteins, LDL Cholesterol: BL, blood
***Lovastatin: AD, administration & dosage**
Middle Age
*Niacin: AD, administration & dosage
*Polyamines: AD, administration & dosage
RN 50925-79-6 (Colestipol); **57-88-5 (Cholesterol)**; 59-67-6 (Niacin); **75330-75-5 (Lovastatin)**
CN 0 (Apolipoproteins B); 0 (Lipoproteins, LDL **Cholesterol**); 0 (Polyamines)

L173 ANSWER 57 OF 63 MEDLINE
AN 87153126 MEDLINE
DN 87153126 PubMed ID: 3644588
TI Comparison of six pharmacologic regimens for **hypercholesterolemia**.
AU Hoeg J M; Maher M B; Bailey K R; Brewer H B Jr
SO AMERICAN JOURNAL OF CARDIOLOGY, **(1987 Apr 1)** 59 (8) 812-5.
Journal code: 3DQ; 0207277. ISSN: 0002-9149.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 198704
ED Entered STN: 19900303
Last Updated on STN: 19900303
Entered Medline: 19870423
AB Six sequential clinical trials were conducted over 5 years to evaluate the safety and efficacy of different treatment regimens for **hypercholesterolemia**. Of all the study participants, 11 patients were evaluated in all 6 clinical trials using the following regimens: neomycin, neomycin/niacin, **cholestyramine**, **cholestyramine**/neomycin, **lovastatin** and **lovastatin**/neomycin. All 6 regimens significantly (p less than 0.05) reduced both total and low-density lipoprotein **cholesterol** concentrations by 25 to 42% from baseline levels. Only neomycin/niacin, **cholestyramine** and **lovastatin** significantly increased the high-density lipoprotein (HDL) **cholesterol** concentration, reducing the total **cholesterol**/high-density lipoprotein **cholesterol** ratio to less than 4.7. Thus, all 6 tested regimens were effective in modifying the plasma lipoprotein concentrations in type II hyperlipoproteinemia, but neomycin/niacin, **cholestyramine** and **lovastatin** had the most favorable impact. Only **lovastatin** treatment was free of adverse effects.
CT Check Tags: Comparative Study; Female; Human; Male
Adult
Aged
Cholestyramine: AE, adverse effects
Cholestyramine: TU, therapeutic use
Drug Therapy, Combination
Hypercholesterolemia: BL, blood
***Hypercholesterolemia: DT, drug therapy**
Hypercholesterolemia, Familial: DT, drug therapy
Lovastatin
Middle Age
Naphthalenes: AE, adverse effects
Naphthalenes: TU, therapeutic use
Neomycin: AE, adverse effects
Neomycin: TU, therapeutic use
Niacin: AE, adverse effects
Niacin: TU, therapeutic use

Retrospective Studies
RN **11041-12-6 (Cholestyramine)**; 1404-04-2 (Neomycin); 59-67-6 (Niacin); **75330-75-5 (Lovastatin)**
CN 0 (Naphthalenes)

L173 ANSWER 58 OF 63 MEDLINE
AN 87061360 MEDLINE
DN 87061360 PubMed ID: 3537351
TI Treatment of primary moderate **hypercholesterolemia** with **lovastatin** (**mevinolin**) and colestipol.
AU Vega G L; Grundy S M
NC HL-29252 (NHLBI)
M01-RR00633 (NCRR)
SO JAMA, **(1987 Jan 2)** 257 (1) 33-8.
Journal code: KFR; 7501160. ISSN: 0098-7484.
CY United States
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 198701
ED Entered STN: 19900302
Last Updated on STN: 19970203
Entered Medline: 19870121
AB The introduction of inhibitors of **cholesterol** biosynthesis offers a new approach to treatment of **hypercholesterolemia**. One such agent, **lovastatin** (formerly, **mevinolin**), causes significant reductions in plasma **cholesterol** levels. This action can be enhanced by bile acid sequestrants. In this study, **lovastatin** and colestipol hydrochloride together were administered to ten patients with primary moderate **hypercholesterolemia**. Compared with a control period, the combined-drug therapy caused a 36% reduction in plasma total **cholesterol** level, a 48% decrease in low-density lipoprotein (LDL) **cholesterol** level, and a 17% increase in high-density lipoprotein **cholesterol** level. The reduction in LDL **cholesterol** level was due to three factors: a 27% decrease in the production rate of LDL, a 20% increase in fractional catabolic rate of LDL, and a 15% depletion of **cholesterol** in LDL particles. This major reduction in LDL **cholesterol** level produced by combined-drug therapy may be valuable for prevention of coronary heart disease in high-risk patients with primary moderate **hypercholesterolemia**.
CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.
Aged
***Anticholesteremic Agents: AD, administration & dosage**
Apolipoproteins: BL, blood
Clinical Trials
*Colestipol: AD, administration & dosage
Drug Therapy, Combination
Hypercholesterolemia: BL, blood
***Hypercholesterolemia: DT, drug therapy**
Kinetics
Lipids: BL, blood
Lipoproteins, HDL Cholesterol: BL, blood
Lipoproteins, LDL Cholesterol: BL, blood
Lovastatin
Middle Age
*Naphthalenes: AD, administration & dosage
*Polyamines: AD, administration & dosage
RN 50925-79-6 (Colestipol); **75330-75-5 (Lovastatin)**
CN 0 (**Anticholesteremic** Agents); 0 (Apolipoproteins); 0 (Lipids); 0 (Lipoproteins, HDL **Cholesterol**); 0 (Lipoproteins, LDL **Cholesterol**); 0 (Naphthalenes); 0 (Polyamines); 0 (apolipoprotein LDL)

L173 ANSWER 59 OF 63 MEDLINE
AN 87041897 MEDLINE
DN 87041897 PubMed ID: 3640503
TI Efficacy of **mevinolin** as adjuvant therapy for refractory familial **hypercholesterolaemia**.
AU Thompson G R; Ford J; Jenkinson M; Trayner I
SO QUARTERLY JOURNAL OF MEDICINE, **(1986 Aug)** 60 (232) 803-11.
Journal code: QKZ; 0401027. ISSN: 0033-5622.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198612
ED Entered STN: 19900302
Last Updated on STN: 19900302
Entered Medline: 19861215
AB **Mevinolin**, a potent inhibitor of **cholesterol** synthesis, was used as a therapeutic adjuvant in patients with refractory familial **hypercholesterolaemia** for an average period of 13 months. Sustained decreases in serum **cholesterol** of 23 and 31 per cent were achieved by doses of 20 mg and 40 mg/day respectively in 13 heterozygotes already on **cholestyramine** or after partial ileal bypass. Administration of 80 mg/day to three patients undergoing plasma exchange reduced peak serum **cholesterol** levels by 11.5 per cent in two homozygotes and by 17 per cent in a double heterozygote for familial **hypercholesterolaemia** and type III hyperlipoproteinaemia. The decrease in **cholesterol** was largely confined to low-density lipoprotein and no significant changes occurred in serum triglyceride or high-density lipoprotein **cholesterol**. **Mevinolin** was well-tolerated except in one patient who developed myositic symptoms; asymptomatic, transient elevations of serum enzymes were observed in five others. Short and long Synacthen tests showed no evidence that the drug impaired adrenocortical response to ACTH. These results indicate that **mevinolin** provides a safe and highly effective means of reducing LDL levels in patients with heterozygous familial **hypercholesterolaemia** refractory to conventional treatment but is less useful in homozygotes.
CT Check Tags: Female; Human; Male
Adult
Aged
Cholesterol: ME, metabolism
Cholestyramine: TU, therapeutic use
Drug Therapy, Combination
Heterozygote
Homozygote
***Hypercholesterolemia, Familial: DT, drug therapy**
Hypercholesterolemia, Familial: ME, metabolism
Hypercholesterolemia, Familial: TH, therapy
Ileum: SU, surgery
Lovastatin
Middle Age
Naphthalenes: AE, adverse effects
*Naphthalenes: TU, therapeutic use
RN **11041-12-6 (Cholestyramine); 57-88-5 (Cholesterol); 75330-75-5 (Lovastatin)**
CN 0 (Naphthalenes)

L173 ANSWER 60 OF 63 MEDLINE
AN 86269217 MEDLINE
DN 86269217 PubMed ID: 3524586
TI The effects of **mevinolin** and neomycin alone and in combination on plasma lipid and lipoprotein concentrations in type II hyperlipoproteinemia.
AU Hoeg J M; Maher M B; Bailey K R; Brewer H B Jr
SO ATHEROSCLEROSIS, **(1986 Jun)** 60 (3) 209-14.
Journal code: 95X; 0242543. ISSN: 0021-9150.

CY Netherlands
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198607
ED Entered STN: 19900321
Last Updated on STN: 19900321
Entered Medline: 19860725
AB The reduction of elevated low density lipoprotein (LDL) **cholesterol** concentrations in patients with Type II hyperlipoproteinemia leads to improved cardiovascular morbidity and mortality. Two agents which may be of value in treating **hypercholesterolemia** are **mevinolin** and neomycin. Since these drugs lower **cholesterol** levels through complementary mechanisms, we evaluated the effects of **mevinolin** and combined **mevinolin**-neomycin treatment on plasma lipoprotein concentrations in 21 type II hyperlipoproteinemic patients. **Mevinolin** reduced total and LDL **cholesterol** concentrations by 24% and 31% respectively (P less than 0.001) and 81% of the patients reduced their LDL **cholesterol** levels to less than 200 mg/dl. Although the addition of neomycin to **mevinolin** treatment further lowered total (5%) and LDL (4%) **cholesterol** concentrations, it also reduced HDL **cholesterol** levels (19%) (P less than 0.05). Therefore **mevinolin** normalizes the plasma lipid concentrations in patients with type II hyperlipoproteinemia and combined **mevinolin** and neomycin treatment offers no advantage over **mevinolin**-only therapy. In addition, these findings emphasize the importance of determining the HDL **cholesterol** level to fully evaluate the effects of hypolipidemic therapy.
CT Check Tags: Human
Clinical Trials
Drug Interactions
Drug Therapy, Combination
Hypercholesterolemia, Familial: BL, blood
Hypercholesterolemia, Familial: DH, diet therapy
***Hypercholesterolemia, Familial: DT, drug therapy**
Lipids: BL, blood
Lipoproteins: BL, blood
Lipoproteins, HDL Cholesterol: BL, blood
Lipoproteins, LDL Cholesterol: BL, blood
Lovastatin
*Naphthalenes: AD, administration & dosage
*Neomycin: AD, administration & dosage
RN 1404-04-2 (Neomycin); **75330-75-5 (Lovastatin)**
CN 0 (Lipids); 0 (Lipoproteins); 0 (Lipoproteins, HDL **Cholesterol**); 0 (Lipoproteins, LDL **Cholesterol**); 0 (Naphthalenes)

L173 ANSWER 61 OF 63 MEDLINE
AN 85277658 MEDLINE
DN 85277658 PubMed ID: 3849281
TI Influence of combined therapy with **mevinolin** and interruption of bile-acid reabsorption on low density lipoproteins in heterozygous familial **hypercholesterolemia.**
AU Grundy S M; Vega G L; Bilheimer D W
NC HL-29252 (NHLBI)
MO1-RR 00633 (NCRR)
SO ANNALS OF INTERNAL MEDICINE, **(1985 Sep)** 103 (3) 339-43.
Journal code: 5A6; 0372351. ISSN: 0003-4819.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 198509
ED Entered STN: 19900320
Last Updated on STN: 19970203

Entered Medline: 19850909
AB Patients with heterozygous familial **hypercholesterolemia** have a 50% deficiency of receptors for plasma low density lipoproteins (LDL) that induces a marked increase in plasma LDL levels. Two therapeutic measures that seem to increase the synthesis of LDL receptors are interruption of the enterohepatic circulation of bile acids with either bile-acid sequestrants or the ileal-exclusion operation, and competitive inhibition of 3-hydroxy-3-methylglutaryl coenzyme A reductase with **mevinolin** or compactin. To determine the effectiveness of this combination and the mechanisms of lowering LDL levels, we measured turnover rates of LDL apoprotein (apo-LDL) before and during treatment with **mevinolin** and colestipol in eight patients with heterozygous familial **hypercholesterolemia**. Drug therapy reduced LDL **cholesterol** levels by an average of 52%; this response was due to a 40% increase in fractional catabolic rate of apo-LDL and a 26% decrease in its production rate. A similar response was obtained in two patients who had previously had an ileal-exclusion operation for severe **hypercholesterolemia** and who were treated with **mevinolin.**
CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.
Adult
Apolipoproteins: BL, blood
*Bile Acids and Salts: ME, metabolism
Cholesterol: BL, blood
Colestipol: TU, therapeutic use
Combined Modality Therapy
Drug Therapy, Combination
Enterohepatic Circulation
Heterozygote
Hydroxymethylglutaryl CoA Reductases: AI, antagonists & inhibitors
Hypercholesterolemia, Familial: BL, blood
Hypercholesterolemia, Familial: DT, drug therapy
***Hypercholesterolemia, Familial: TH, therapy**
Ileum: SU, surgery
Kinetics
***Lipoproteins, LDL: BL, blood**
Lovastatin
Middle Age
*Naphthalenes: TU, therapeutic use
RN 50925-79-6 (Colestipol); **57-88-5 (Cholesterol); 75330-75-5 (Lovastatin)**
CN 0 (Apolipoproteins); 0 (Bile Acids and Salts); 0 (Lipoproteins, LDL); 0 (Naphthalenes); 0 (apolipoprotein LDL); EC 1.1.1.88 (Hydroxymethylglutaryl CoA Reductases)

L173 ANSWER 62 OF 63 MEDLINE
AN 85041661 MEDLINE
DN 85041661 PubMed ID: 6388097
TI **Mevinolin** stimulates receptor-mediated clearance of low density lipoprotein from plasma in familial **hypercholesterolemia** heterozygotes.
AU Bilheimer D W; Grundy S M; Brown M S; Goldstein J L
NC HL-15949 (NHLBI)
HL-20948 (NHLBI)
HL-29252 (NHLBI)
SO TRANSACTIONS OF THE ASSOCIATION OF AMERICAN PHYSICIANS, **(1983)** 96 1-9. Ref: 14
Journal code: W5P; 7506109. ISSN: 0066-9458.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LA English
FS Priority Journals
EM 198412
ED Entered STN: 19900320
Last Updated on STN: 19970203

Entered Medline: 19841218

AB The current results show that one can exploit the normal regulation of receptor synthesis to stimulate the single normal gene in FH heterozygotes to produce an increased number of LDL receptors. This stimulation can be achieved by drugs that inhibit HMG CoA reductase in the liver and by maneuvers that cause bile acid depletion. These two therapeutic approaches are most effective when they are combined. It seems reasonable to speculate that such a profound lowering of plasma **cholesterol** levels will minimize the development of atherosclerosis in FH heterozygotes. In a broader sense, the success of this regulatory manipulation raises the possibility that other genetic diseases may be treated through manipulation of regulatory signals that control the rates of synthesis of gene products.

CT Check Tags: Animal; Human; Support, U.S. Gov't, P.H.S.
Anticholesteremic Agents: PD, pharmacology
***Anticholesteremic Agents: TU, therapeutic use**
Cholesterol: BI, biosynthesis
Colestipol: TU, therapeutic use
Combined Modality Therapy
Dogs
Drug Therapy, Combination
Heterozygote
Hypercholesterolemia, Familial: BL, blood
***Hypercholesterolemia, Familial: DT, drug therapy**
Hypercholesterolemia, Familial: GE, genetics
Hypercholesterolemia, Familial: SU, surgery
Ileum: SU, surgery
***Lipoproteins, LDL: BL, blood**
Lipoproteins, LDL Cholesterol: BL, blood
Liver: ME, metabolism
Lovastatin
Naphthalenes: PD, pharmacology
*Naphthalenes: TU, therapeutic use
*Receptors, LDL: BI, biosynthesis

RN 50925-79-6 (Colestipol); **57-88-5 (Cholesterol)**; **75330-75-5 (Lovastatin)**

CN 0 (**Anticholesteremic** Agents); 0 (Lipoproteins, LDL); 0 (Lipoproteins, LDL **Cholesterol**); 0 (Naphthalenes); 0 (Receptors, LDL)

L173 ANSWER 63 OF 63 MEDLINE
AN 85020945 MEDLINE
DN 85020945 PubMed ID: 6567462
TI **Mevinolin** plus colestipol in therapy for severe heterozygous familial **hypercholesterolemia**.
AU Illingworth D R
NC HL29074 (NHLBI)
HL32271 (NHLBI)
RR334 (NCRR)
+
SO ANNALS OF INTERNAL MEDICINE, **(1984 Nov)** 101 (5) 598-604.
Journal code: 5A6; 0372351. ISSN: 0003-4819.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 198411
ED Entered STN: 19900320
Last Updated on STN: 19970203
Entered Medline: 19841114

AB Twelve patients with severe heterozygous familial **hypercholesterolemia**, in whom other hypolipidemic drug therapy had failed to reduce serum **cholesterol** levels to less than 300 mg/dL, were sequentially treated with **mevinolin** (a specific inhibitor of 3-hydroxy-3-methylglutaryl coenzyme A reductase, the rate-limiting enzyme in **cholesterol** biosynthesis) and

colestipol. In ten patients receiving 80 mg/d of **mevinolin**, plasma **cholesterol** concentrations decreased 33%, from 487 +/- 27 (SE) mg/dL to 326 +/- 16 mg/dL. Additional therapy with colestipol resulted in a further 18% decrease, to 269 +/- 13 mg/dL. Concentrations of low density lipoprotein (LDL) **cholesterol** decreased in parallel (54% decrease on combined drug therapy). Plasma concentrations of high density lipoprotein **cholesterol** did not change significantly, but the LDL:HDL ratio decreased from 8.2 in patients on diet only to 3.8 in patients treated with **mevinolin** and colestipol. In seven patients treated with 40 mg/d of **mevinolin**, concentrations of LDL **cholesterol** decreased by 33%; combined therapy resulted in a further 20% decrease (46% reduction from the level achieved with diet only). No consistent side effects have been noted in up to 24 months of therapy. Combined therapy with **mevinolin** and colestipol promises to be effective for heterozygous familial **hypercholesterolemia**.

CT Check Tags: Female; Human; Male; Support, U.S. Gov't, P.H.S.
Adult
Aged
Anticholesteremic Agents: AD, administration & dosage
***Anticholesteremic Agents: TU, therapeutic use**
Cholesterol: BL, blood
Colestipol: AD, administration & dosage
*Colestipol: TU, therapeutic use
Drug Therapy, Combination
Heterozygote
Hypercholesterolemia, Familial: BL, blood
***Hypercholesterolemia, Familial: DT, drug therapy**
Lipoproteins, HDL Cholesterol: BL, blood
Lipoproteins, LDL Cholesterol: BL, blood
Lovastatin
Middle Age
Naphthalenes: AD, administration & dosage
*Naphthalenes: TU, therapeutic use
*Polyamines: TU, therapeutic use

RN 50925-79-6 (Colestipol); **57-88-5 (Cholesterol)**; **75330-75-5 (Lovastatin)**

CN 0 (**Anticholesteremic** Agents); 0 (Lipoproteins, HDL **Cholesterol**); 0 (Lipoproteins, LDL **Cholesterol**); 0 (Naphthalenes); 0 (Polyamines)

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L219 ANSWER 1 OF 5  WPIX   COPYRIGHT 2001   DERWENT INFORMATION LTD
AN   1996-230977 [24]   WPIX
DNC  C1996-073056
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TI Pure high mol. wt. **sulphated polysaccharide** prepn. - by filtering and diafiltering aq. mixt. contg. crude prod, used as **cholesterol esterase** inhibitor and **hypocholesterolaemic** agent.

DC B04 D13

IN LANGE, L G; REARDAN, D T; SPILBURG, C A

PA (CVTH-N) CV THERAPEUTICS INC

CYC 21

PI AU 9534240 A 19960426 (199624)* 60p C08B005-14
EP 712864 A2 19960522 (199625) EN 26p C08B037-00
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
US 5521303 A 19960528 (199627) 18p C07H001-06
CA 2160440 A 19960414 (199633) C08B005-14
EP 712864 A3 19961016 (199648) C08B005-14
JP 08253502 A 19961001 (199649) 21p C08B037-00
JP 2655592 B2 19970924 (199743) 21p C08B037-00
AU 682792 B 19971016 (199801) C08B005-14
CA 2160440 C 19980825 (199845) C08B005-14

ADT AU 9534240 A AU 1995-34240 19951012; EP 712864 A2 EP 1995-307295 19951013; US 5521303 A US 1994-322782 19941013; CA 2160440 A CA 1995-2160440 19951012; EP 712864 A3 EP 1995-307295 19951013; JP 08253502 A JP 1995-265885 19951013; JP 2655592 B2 JP 1995-265885 19951013; AU 682792 B AU 1995-34240 19951012; CA 2160440 C CA 1995-2160440 19951012

FDT JP 2655592 B2 Previous Publ. JP 08253502; AU 682792 B Previous Publ. AU 9534240

PRAI US 1995-451563 19950526; US 1994-322782 19941013

REP No-SR.Pub; EP 53473; WO 9012579

IC ICM C07H001-06; C08B005-14; C08B037-00
ICS A23L001-30; **A61K031-72**; **A61K031-725**; C08B003-00

AB AU 9534240 A UPAB: 19960618
Prepn. of a non-absorbable, very high mol.wt. **sulphated polysaccharide** (I), having **sulphate** to monomer ratio 1.0-3.0, contg. < 5.0 wt.% **sulphates polysaccharides** of mol.wt. < 75000 and contg. < 0.5 wt.% inorganic **sulphate**, involves: (a) admixing water with a dry crude high mol.wt., **sulphated polysaccharide** (II); (b) filtering the obtd. aq. (II) soln.; and (c) diafiltering the filtrate against water using a membrane of mol.wt. cut-off 500000 or more.

A new (I), having **sulphate** to monomer ratio 2 and average mol.wt. > 2000000, i.e. (I'), is obtd. as above, where the crude starting material (II) has been prepd. by adding DMF/SO3 complex to a suspension reaction at below 20deg.C, adding aq. base and sepg. (II) from DMF and aq. reactants by washing the mixt. with an organic solvent such as acetone.

Also claimed are: a method of lowering serum **cholesterol** (Ch) in humans by admin. of (I) (specifically (I')) by ingestion; an inhibitor of human Ch absorption comprising a therapeutic amt. of (I); and an inhibitor of human **cholesterol esterase** (CE) comprising 10-5000 mg (I').

USE - (I) specifically inhibit or decrease intestinal Ch absorption by inhibiting pancreatic CE-catalysed hydrolysis of naturally occurring and ingested Ch esters and by inhibiting CE-facilitated free Ch uptake.

(I) may be used as drugs or as dietary supplements (esp. with foods rich in Ch and/or its esters) to reduce Ch absorption.

Therapeutic dose of (I) is 10-5000 mg, pref. incorporated into a food prodn. or administered in a pharmaceutical dosage form selected from tablets, capsules, liquids and powder.

ADVANTAGE - (I) are potent (Ki < 5 muM) and safe CE inhibitors. They are not absorbed, do not activate the plasma enzyme lipoprotein lipase and are non-degradable, non-toxic and inexpensive, being derived from cheap (possibly waste) materials.

The process eliminates toxic low mol.wt. **polysaccharide** and free **sulphate** by-prods.

(I) do not cause steatorrhoea.

Dwg.0/4

FS CPI

FA AB; DCN

MC CPI: **B04-C02**; **B14-D02A2**; B14-D07A; B14-F06; D03-H01T2
ABEQ US 5521303 A UPAB: 19960710
A process for preparing an essentially non-absorbable very high molecular weight **sulphated polysaccharide** having less than about 5.0 wt. percent of **sulphated polysaccharides** having a molecular weight less than 75,000 Daltons, and containing less than 0.5 weight percent of inorganic **sulphate**, comprising the steps;
(a) admixing water with a dry crude high molecular weight **sulphated polysaccharide** to create a crude aqueous **sulphated polysaccharide** solution;
(b) filtering the crude aqueous **sulphated polysaccharide** solution in a first filtering step to produce a filtrate; and
(c) dia-filtering the filtrate of step (b) against water using a membrane having a molecular weight cut-off of 500,000 or greater in a second filtering step to produce a purified very high molecular weight **sulphated polysaccharide**.
Dwg.0/0

L219 ANSWER 2 OF 5 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1996-087083 [09] WPIX
CR 1990-348258 [46]; 1991-178095 [24]
DNC C1996-028151
TI 3-**Sulphated-polysaccharide cholesterol esterase** inhibitor - in baked food product.
DC B04 D13
IN LANGE, L G; SPILBURG, C A
PA (LANG-I) LANGE L G; (SPIL-I) SPILBURG C A
CYC 1
PI US 5484777 A 19960116 (199609)* 9p A61K031-72 <--
ADT US 5484777 A CIP of US 1989-340868 19890420, Cont of US 1991-718280 19910620, Cont of US 1992-928510 19920811, US 1993-167725 19931215
FDT US 5484777 A CIP of US 5017565
PRAI US 1991-718280 19910620; US 1989-340868 19890420; US 1992-928510 19920811; US 1993-167725 19931215
IC ICM **A61K031-72**
AB US 5484777 A UPAB: 19991221
An ingestible food product comprises a foodstuff and a therapeutic amount of a non-absorbable synthetic 3-**sulphated polysaccharide** having an IC50 of 0.02nM or less and a MW of at least 500 kDa, the product being baked.
USE - The **sulphated polysaccharide** inhibits human pancreatic **cholesterol esterase**, thereby decreasing intestinal absorption of **cholesterol** and fatty acid.
Dwg.0/3
FS CPI
FA AB; GI
MC CPI: **B04-C02**; B14-D07A; B14-F06; D03-H01T2

L219 ANSWER 3 OF 5 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1990-348258 [46] WPIX
CR 1991-178095 [24]; 1996-087083 [09]
DNC C1990-151144
TI Inhibition of intestinal **cholesterol** absorption - by oral admin of non-absorbable inhibitor of **cholesterol esterase**, esp. high mol.wt. **sulphated polysaccharide**.
DC B04 D16
IN LANGE, L G; SPILBURG, C A
PA (LANG-I) LANGE L G; (SPIL-I) SPILBURG C A; (SCHI-I) SCHIERANO P
CYC 17
PI WO 9012579 A 19901101 (199046)* 49p
RW: AT BE CH DE DK ES FR GB IT LU NL SE
W: AU CA JP US
AU 9055356 A 19901116 (199107)
US 5017565 A 19910521 (199123) 8p
US 5063210 A 19911105 (199147) 11p

EP 469079 A 19920205 (199206)
R: AT BE CH DE ES FR GB IT LI LU NL SE
JP 04503813 W 19920709 (199234) 19p A61K045-00 <--
AU 633569 B 19930204 (199312) A61K031-715 <--
EP 469079 B1 19941207 (199502) EN 29p A61K031-72 <--
R: AT BE CH DE DK ES FR GB IT LI LU NL SE
DE 69014870 E 19950119 (199508) A61K031-72 <--
ES 2064736 T3 19950201 (199511) A61K031-72 <--
JP 08019001 B2 19960228 (199613) 19p A61K045-00 <--
US 5616570 A 19970401 (199719)# 20p A61K031-72 <--
CA 2053258 C 19980210 (199817) A61K031-72 <--
US 5792832 A 19980811 (199839) C07K007-06

ADT US 5017565 A US 1989-340868 19890420; US 5063210 A US 1989-429398 19891031; EP 469079 A EP 1990-907923 19900420; JP 04503813 W JP 1990-506819 19900420, WO 1990-US2079 19900420; AU 633569 B AU 1990-55356 19900420; EP 469079 B1 EP 1990-907923 19900420, WO 1990-US2079 19900420; DE 69014870 E DE 1990-614870 19900420, EP 1990-907923 19900420, WO 1990-US2079 19900420; ES 2064736 T3 EP 1990-907923 19900420; JP 08019001 B2 JP 1990-506819 19900420, WO 1990-US2079 19900420; US 5616570 A Cont of WO 1990-US2079 19900420, Cont of US 1991-773875 19911018, US 1994-283723 19940801; CA 2053258 C CA 1990-2053258 19900420; US 5792832 A Cont of US 1989-429398 19891031, Cont of US 1989-434899 19891113, Cont of US 1992-856910 19920512, Div ex US 1994-350801 19941207, US 1995-461881 19950605

FDT JP 04503813 W Based on WO 9012579; AU 633569 B Previous Publ. AU 9055356, Based on WO 9012579; EP 469079 B1 Based on WO 9012579; DE 69014870 E Based on EP 469079, Based on WO 9012579; ES 2064736 T3 Based on EP 469079; JP 08019001 B2 Based on JP 04503813, Based on WO 9012579; US 5792832 A Cont of US 5173408

PRAI US 1989-429398 19891031; US 1989-340868 19890420; US 1994-283723 19940801; US 1989-434899 19891113; US 1992-856910 19920512; US 1994-350801 19941207; US 1995-461881 19950605

REP 2.Jnl.Ref; DE 1492011; GB 1053143; GB 953626; US 3148114; US 4520017; 01Jnl.Ref; GB 1164569; GB 1433732; US 3175942; US 4436731; US 4623539

IC ICM **A61K031-715**; **A61K031-72**; **A61K045-00**; C07K007-06
ICS A23L001-30; A23L001-308; **A61K031-725**; **A61K031-73**; **A61K031-795**; **A61K039-39**; **A61K039-395**; C07K009-00; C12N009-16

ICA C12N009-99

AB WO 9012579 A UPAB: 19991221
Ingestible food prod. contains an effective amt. of a non-absorbable synthetic **cholesterol esterase** inhibitor (I).
Inhibiting the intestinal absorption of **cholesterol** comprises admin. p.o. a non-absorbable inhibitor of **cholesterol esterase** or an antibody directed against **cholesterol esterase**.
Reducing serum **cholesterol** levels comprises admin. of a synthetic non-absorbable **sulphated polysaccharide** in combination with an absorbed **cholesterol** synthesis blocker, triglyceride lipase inhibitor or fatty acyl **cholesterol** O-acyl transferase (ACAT) inhibitor.
USE/ADVANTAGE - (I), esp. **sulphonated polysaccharides**, decrease intestinal absorption of **cholesterol** and fatty acid by inhibiting pancreatic **cholesterol esterase**, which is a key enzyme involved in dietary **cholesterol** absorption. (I) are stable and can be incorporated in food prods., including baked prods. for dietary control of serum **cholesterol** levels and atherosclerosis (I) are potent inhibitors; are non-absorbable, so that side-effects are reduced; and are inexpensive. Doses of **cholesterol** synthesis blockers or ACAT inhibitors can be reduced, and side-effects minimized, by use with (I).
Dwg.0/10

FS CPI

FA AB

MC CPI: B04-B04C6; B04-B04F; **B04-C02**; B07-A02; B12-G01B2;

B12-G01B3; **B12-H03**; B12-J01; D03-H01T

ABEQ US 5017565 A UPAB: 19930928
Method of inhibiting human pancreatic **cholesterol esterase** in the alimentary tract comprises oral admin. of a 3-**sulphated polysaccharide** (I). (I) is pref. 3-**sulphated** alginic acid, pectin, amylopectin, chitin, dextran, cellulose agar or chitosan which are all soluble, potent inhibitors of human pancreatic **cholesterol esterase**.
USE - In inhibiting or decreasing **cholesterol** and fatty acid absorption.
In an example, Na alginate (150 mg) was treated with 5 cc glacial acetic acid for 2 hrs. at room temp., filtered and resuspended in 5 ml N,N-dimethylformamide. To stirred soln. 1.5 g SO3-pyridine complex was added over 30 mins. at room temp. and resulting mixt. stirred overnight for 16 hrs. 5 ml dry pyridine was then added and the **sulphated** alginic acid was pptd. with 10 ml acetone-MeOH (9:1) mixt. before dissolving in 50 ml H2O and adding IN NaOH to adjust pH to 8. Repptn. with 200 ml acetone-MeOH (9:1) mixt. produced the Na salt of **sulphonated** alginic acid. Cpd. was tested for **cholesterol esterase** inhibition and it had IC50 of 0.25 microg/ml or 1.0nM.

ABEQ US 5063210 A UPAB: 19930928
Inhibiting pancreatic **cholesterol esterase** comprises contacting it with a 3-**sulphate polysaccharide** of M.W. 10+ kDa (100+ kDa, 500+ kDa). Pref. the 3-**sulphated polysaccharide** is 3-**sulphated** alginic acid, pectin, amylopectin, chitin, dextran, cellulose, agar or chitosan (Fig.2). Prepn. is e.g. by treating chitosan with glacial HOAc, dissoln.e in DMFA and sulphation with SO3/pyridine.
USE - The method reduces the absorption of **cholesterol** and triglycerides from the intestine and their concns. in the blood stream so reducing risk of atherosclerosis, etc. The material can be eaten in a baked biscuit.

ABEQ EP 469079 B UPAB: 19950117
Use of a non-absorbable inhibitor of **cholesterol esterase** in the manufacture of an ingestible pharmaceutical compostion for inhibiting the intestinal absorption of **cholesterol** wherein said inhibitor is a 3-**sulphated polysaccharide** or an antibody to **cholesterol esterase**.
Dwg.0/7

ABEQ US 5616570 A UPAB: 19970512
A method for inhibiting the intestinal absorption of **cholesterol** in a mammal by administering orally a non-absorbable inhibitor of **cholesterol esterase** comprising a 3-**sulphated polysaccharide** having a molecular weight greater than 100,000 Da.
Dwg.0/7

L219 ANSWER 4 OF 5 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1990-218740 [29] WPIX
DNN N1990-169759 DNC C1990-094452
TI Determn. of net high density lipoprotein **cholesterol** content of serum - by pptn. of other lipoprotein(s) then assaying **cholesterol** in lipase treated and untreated samples, for assessing risk of vascular disease.
DC B04 D13 S03
IN MAINES, R Q
PA (MAIN-I) MAINES R Q
CYC 14
PI EP 378395 A 19900718 (199029)*
R: AT BE CH DE ES FR GB LI LU NL SE
CA 2007645 A 19900713 (199039)
EP 378395 A3 19920701 (199333)
US 5453358 A 19950926 (199544) 5p C12Q001-60
EP 378395 B1 19960814 (199637) EN 12p C12Q001-60
R: AT BE CH DE DK ES FR GB LI LU NL SE
DE 69028023 E 19960919 (199643) C12Q001-60
ADT EP 378395 A EP 1990-300287 19900110; EP 378395 A3 EP 1990-300287 19900110;

US 5453358 A Cont of US 1989-297080 19890113, US 1992-941669 19920908; EP 378395 B1 EP 1990-300287 19900110; DE 69028023 E DE 1990-628023 19900110, EP 1990-300287 19900110
FDT DE 69028023 E Based on EP 378395
PRAI US 1989-297080 19890113; US 1992-941669 19920908
REP NoSR.Pub; 6.Jnl.Ref; EP 271963; GB 2097255; JP 51139634; JP 61118323; JP 62263119; US 4186251; US 4215993; US 4414326; WO 8905354
IC **A61K031-68**; C12Q001-60; G01N033-92
ICM C12Q001-60
ICS **A61K031-23**; **A61K031-68**; **A61K031-685**
ICA G01N033-92
AB EP 378395 A UPAB: 19931119
Determin. of the net HDL **cholesterol** content of blood serum comprises (1) treating a sample with a pptg. agent which combines with LDL and VLDL particles in the serum; (2) centrifuging to remove ppte., leaving supernatant contg. HDL and free **cholesterol** (ch); (3) treating supernatant with enzyme which de-esterifies (ch), so as to break down HDL particles into (Ch) and fatty acid; (4) treating with (Ch) oxidase to oxidise all (Ch)to H2O2 and cholest-4-en-3-one; (5) treating with peroxidase (POD), 4-amine-antipyrine (4AAP) and chromogen to convert the H2O2 producedto a quinone imine (QI); (6) measuring the absorbance of QI at a suitable wavelength; (7) repeating steps (3-6) on at least one (Ch)-contg. standard; (8) calculating the concn. of HDL and non-pptd. (Ch) from the equation (HDL + free (Ch) concn.) = S.C. x 2As/Ast. (As and Ast = absorbance of sample and standard respectively; S.C = concn. of the standard); (9) repeating steps (4-6) on separate samples of supernatant and standard, (10) calculating the non-pptd. free (Ch) concn. from the eqn. free (Ch) concn. = S.C. x 2As/Ast and (11) calculating net HDL **cholesterol** by subtraction of results from steps (8) and (10).

Also new is an emulsified diet supplement for increasing % HDL **cholesterol** in the blood consisting of a polyunsatd. lipid, phospholipid contg. essential fatty acids; a polysaccharide and an antioxidant.

USE - The measurement of HDL **cholesterol** is used to diagnose (and assess the risk of) vascular disease and atherosclerosis. The new diet supplement reduces the risk of such diseases. @(9pp Dwg.No.0/0)

0/0
FS CPI EPI
FA AB; DCN
MC CPI: B01-D02; B03-F; B03-H; B04-B01B; B04-B01C1; B04-B02C2; B04-B02C3; B04-B04D4; **B04-C02D**; B04-C03D; B05-B01P; B07-D08; B10-C03; B11-C07B1; **B12-H03**; B12-K04A; D03-C; D05-A02A; D05-A02C
EPI: S03-E14H
ABEQ US 5453358 A UPAB: 19951109
Determining the level of risk for a patient to vascular disease comprises (a) determining the net percentage of HDL **cholesterol** of blood serum by (i) precipitating LDL and VLDL fractions from a blood serum sample, (ii) sepg. and isolating the precipitant from a supernatant, (iii) treating the supernatant with **cholesterol esterase** or lipase to de-esterify HDL **cholesterol**, (iv) converting all of the **cholesterol** in the supernatant to H2O2 and cholest-4-en-3-one, (v) converting all H2O2 to quinoneimine in the supernatant, (vi) determining the amt. of quinoneimine in the supernatant, (vii) converting the amt. into a concn. of HDL **cholesterol** and free **cholesterol**, (viii) effecting steps (iv)-(vi) on a 2nd sample of the supernatant from step (ii) and converting the amt. into a concn. of free **cholesterol**, and (ix) determining net HDL **cholesterol** by subtracting the concn. of free **cholesterol** from step (viii) from the concn. of HDL **cholesterol** and free **cholesterol** from step (vii), and (b) determining an increased risk of vascular disease for patients exhibiting concns. of net HDL **cholesterol** that are less than 15% of total serum **cholesterol**.

USE - The method is also used for diagnosing atherosclerosis.
Dwg.0/0

ABEQ EP 378395 B UPAB: 19960918
A method of determining the net concentration of **cholesterol** associated with HDL particles in blood serum, comprising the steps of (a) treating a sample of the serum with a precipitating agent which will combine with the LDL and VLDL particles in the serum; (b) centrifuging the treated serum sample until the LDL- and VLDL-containing precipitate is spun down, leaving a supernatant liquid having HDL associated **cholesterol**, and free supernatant **cholesterol**; (c) separating the supernatant liquid from the precipitate; (d) treating a fist sample of the supernatant liquid with **cholesterol** **esterase** or lipase in sufficient quantity to break down all the HDL particles into fee **cholesterol** and fatty acids, resulting in a **cholesterol**-containing fluid having no esterified **cholesterol**; (e) treating the **cholesterol**-containing fluid with **cholesterol** oxidase in sufficient quantity to oxidise all the **cholesterol** present, forming hydrogen peroxide and cholest-4-en-3-one; (f) further treating the fluid with peroxidase, 4-aminoantipyrine and a chromogen in sufficient amounts to completely react all the hydrogen peroxide formed in step (e) to produce a quinoneimine; (g) measuring the electromagnetic radiation absorbance of the quinonimine-containing fluid produced in step (h) at a wavelength at which the quinonimine exhibits significant absorbance; (i) performing steps (d) through (g) on each of one or more standard **cholesterol** -containing fluids; (j) calculating the combined concentration of **cholesterol** associated with the HDL particles, and free supernatant **cholesterol** according to the formula (**cholesterol** associated with HDL + free supernatant **cholesterol** concentration) = standard concentration x 2(Asupernatant)/A standard, where Asupernatant represents the absorbance measured for the supernatant and Astandard represents the absorbance measured for the standard **cholesterol**-containing fluid; (k) performing steps (e) through (g) on a second sample of the supernatant liquid, and one or more standard **cholesterol**-containing fluids, (l) calculating the concentration of free supernatant **cholesterol** from the absorbance values obtained in step (j) according to the formula free supernatant **cholesterol** concentration = 2(Asupernatant)/Astandard x standard concentration; and (m) calculating the net concentration of **cholesterol** associated with HDL particles from the results of steps (i) and (k) according to the formula net concentration of **cholesterol** associated with HDL = (**cholesterol** associated with HDL + free supernatant **cholesterol** concentration) - free supernatant **cholesterol** concentration.
Dwg.0/0

L219 ANSWER 5 OF 5 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1989-292337 [40] WPIX
DNC C1989-129545
TI Inhibition of intestinal **cholesterol** and fatty acid absorption - by admin. of heparin, its sub-fraction or heparinase.
DC B04 D16
IN KINNUNEN, P M; LANGE, L G; SPILBURG, C A
PA (LANG-I) LANGE L G; (CVTH-N) CV THERAPEUTICS; (JEWI-N) JEWISH HOSPITAL ST
CYC 13
PI WO 8908456 A 19890921 (198940)* 35p
RW: AT BE CH DE FR GB IT LU NL SE
W: AU JP
AU 8934348 A 19891005 (199001)
US 5352601 A 19941004 (199439) 14p C12N009-16
US 5429937 A 19950704 (199532) 13p C12N009-16
US 5492822 A 19960220 (199613) 12p C12N009-16
ADT WO 8908456 A WO 1989-US787 19890227; US 5352601 A CIP of US 1988-168424 19880315, Cont of US 1989-312255 19890222, Cont of US 1990-544212 19900626, Cont of US 1991-655289 19910214, US 1992-936103 19920826; US 5429937 A CIP of US 1988-168424 19880315, Cont of US 1989-312255 19890222, Cont of US 1990-544212 19900626, Cont of US 1991-655289 19910214, Div ex

US 1992-936103 19920826, US 1994-311862 19940926; US 5492822 A CIP of US 1988-168424 19880315, Cont of US 1989-312255 19890222, Cont of US 1990-544212 19900626, Cont of US 1991-655289 19910214, Div ex US 1992-936103 19920826, Div ex US 1994-311862 19940926, US 1995-386433 19950210

FDT US 5429937 A Div ex US 5352601; US 5492822 A Div ex US 5352601, Div ex US 5429937

PRAI US 1989-312255 19890222; US 1988-168424 19880315; US 1990-544212 19900626; US 1991-655289 19910214; US 1992-936103 19920826; US 1994-311862 19940926; US 1995-386433 19950210

IC **A61K031-70; A61K037-48**

ICM C12N009-16

ICS **A61K031-70; A61K037-48; A61K037-54**

AB WO 8908456 A UPAB: 19930923

Inhibiting intestinal cell endogenous heparin mediated absorption of **cholesterol** or fatty acids in mammals comprises orally administering heparin, an active heparin subfraction or heparinase.

USE - Heparin can compete for binding to **cholesterol esterase**, displacing the enzyme from the membrane of the intestinal cell and greatly diminishing the intestinal absorption of **cholesterol** and **cholesterol** derived fatty acids. Also exogenous heparin displaces the pancreatic enzymes, such as triglyceride lipase which hydrolyse triglycerides into free fatty acids, from the membrane of the intestinal cell.

6

FS CPI

FA AB; DCN

MC CPI: B04-B02C2; **B04-C02E1**; **B12-H03**; D05-H10

ABEQ US 5352601 A UPAB: 19941122

Recovery of purified human pancreatic **cholesterol esterase** fraction (Mr 52,000) comprises passing a soln. of the crude esterase (pH about 8.2) over or through 2-(diethylamino)ethyl-cellulose, when other esterases are bonded to the solid phase; and collecting the eluate contg. the required fraction. Opt. further purification is possible by binding impurities on hydroxyapatite and heparin-Sepharose adsorbents.

USE/ADVANTAGE - The enzyme catalyses the cleavage of **cholesterol** esters in the presence of heparin, heparinase or their active fragments, inhibiting the absorption of **cholesterol** or fatty acids in intestinal cells. The oral administration of heparin or heparinase provides prophylaxis and therapy for atherosclerosis.

Dwg.0/0

ABEQ US 5429937 A UPAB: 19950818

Soln. of purified human pancreatic **cholesterol esterase** of mol.wt. 100000 is prepd. from a dialysed soln. contg. protein impurities and similar **cholesterol esterase** protein of various mol.wt. Process comprises (a) chromatographing the soln. obtd. on heparin agarose; (b) washing the impurities away; and (c) eluting and collecting the band contg. prod. of mol.wt. 100000.

USE - Used for inhibiting intestinal **cholesterol** absorption in mammals, and in the treatment of atherosclerosis.

Dwg.0/6

ABEQ US 5492822 A UPAB: 19960329

A method for recovering a solution of purified human pancreatic **cholesterol esterase** having a molecular weight of about 100,000, daltons comprising the steps:

(a) preparing a solution of dialysed human pancreatic cytosol including at least two molecular weight fractions of human pancreatic **cholesterol esterase**, one of which is the 100,000 daltons molecular weight fraction of human **cholesterol esterase**;

(b) passing the solution of dialysed pancreatic cytosol over a hydroxyapatite column and eluting all molecular weight fractions of **cholesterol esterase** present as a single peak to give a first eluent;

(c) passing the first eluent over a gel filtration column and

collecting the 100,000 molecular weight fraction of **cholesterol esterase** as a single peak to give a second eluent including the 100,000 dalton molecular weight fraction of **cholesterol esterase** and protein impurities;

(d) dialysing the second eluent;

(e) passing the dialysed second eluent over a chromatography column containing a chromatography material selected from the group consisting of heparin agarose and heparin-Sepharose: and

(f) washing the chromatography column of step (e) and collecting a third eluent containing the purified **cholesterol esterase** having a molecular weight of about 100,000 daltons.

Dwg.0/6

=> d all abeq tech tot

L224 ANSWER 1 OF 9 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2001-049789 [06] WPIX
DNC C2001-013643
TI Treatment of **hypercholesterolemia** with an unsubstituted polydiallylamine polymer and a **cholesterol**-lowering agent.
DC A96 B05
IN DHAL, P K; HOLMES-FARLEY, S R; HUVAL, C C; PETERSEN, J S
PA (GELT-N) GELTEX PHARM INC
CYC 85
PI WO 2000069445 A1 20001123 (200106)* EN 33p A61K031-785 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZA ZW
AU 9939880 A 20001205 (200113) A61K031-785 <--
ADT WO 2000069445 A1 WO 1999-US10568 19990513; AU 9939880 A AU 1999-39880 19990513, WO 1999-US10568 19990513
FDT AU 9939880 A Based on WO 200069445
PRAI WO 1999-US10568 19990513
IC ICM **A61K031-785**
ICS **A61K045-06**; A61P009-10
AB WO 200069445 A UPAB: 20010126
NOVELTY - Treatment of **hypercholesterolemia** comprises administration of an unsubstituted polydiallylamine polymer (I) and a **cholesterol**-lowering agent (II).

DETAILED DESCRIPTION - Treatment of **hypercholesterolemia** comprises administration of an unsubstituted polydiallylamine polymer (I) and a **cholesterol**-lowering agent (II).

An INDEPENDENT CLAIM is included for the following:

(1) a composition comprising (I) and (II) and optionally a carrier.

ACTIVITY - **Antihypercholesterolemic**

MECHANISM OF ACTION - Bile sequestrants; **Cholesterol** inhibitor

USE - For treatment of **hypercholesterolemia** and atherosclerosis and for reducing serum **cholesterol**

Dwg.0/0
FS CPI
FA AB; GI; DCN
MC CPI: A04-B; A12-V01; B04-C03B; B04-C03D; B07-D03; B07-D05; **B14-D02A2**
TECH UPTX: 20010126
TECHNOLOGY FOCUS - PHARMACEUTICALS - (II) is a fibrate, nicotinic acid or its derivatives, acifran, azacosterol, benfluorex, approximatelyB-benzalbutyramide, carnitine, chondroitin **sulfate**, clomestrone, deyaxtran, **dextran sulfate** sodium, 5,8,11,14,17-eicosapentaenoic acid, eritadenine, furazabol, meglutol, melinamide, mytatrienediol, ornithine, gamma-oryzanol, pantethine, pentaerythritol tetraacetate, alpha-phenylbutyramide, priozadil, probucol,

B-sitosterol, sultosilic acid, piperazine salt, tiadenol, triparanol and/or xenbucin, preferably a fibrate, especially clofibrate, gemfibrozil, fenofibrate and/or bezafibrate, niacin or probucol.

TECHNOLOGY FOCUS - POLYMERS - (I) comprises monomeric units of formula (a) and/or (b) or their salts.
A = A bond or CH2
. The polymer is cross-linked by means of 0.5-50 (preferably 2.5-20) weight% a multifunctional cross-linking agent, preferably epichlorohydrin, bis(diallylammonium)dialkylene ion. The polymer is a homo or copolymer, preferably comprising diallylamine, allylamine and triallylamine monomers, especially diallylamine and allylamine monomers.

L224 ANSWER 2 OF 9 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2000-182534 [16] WPIX
CR 2000-171407 [14]; 2000-182521 [14]; 2000-182522 [14]; 2000-182541 [14]; 2000-182547 [14]; 2000-182548 [14]; 2000-205366 [14]
DNC C2000-057146
TI Antilipemic composition used for lowering **cholesterol** comprises anionic **polysaccharide** material containing non-**sulfated** glucuronic acid.
DC A96 B04
IN BRIESTENSKY, J; KISS, F; SANTAR, I
PA (ALPE-N) ALPENSTOCK HOLDINGS LTD
CYC 87
PI WO 2000004907 A1 20000203 (200016)* EN 49p A61K031-715 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW
AU 9950620 A 20000214 (200029) A61K031-715 <--
EP 1098654 A1 20010516 (200128) EN A61K031-715 <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
ADT WO 2000004907 A1 WO 1999-IE70 19990721; AU 9950620 A AU 1999-50620 19990721; EP 1098654 A1 EP 1999-935019 19990721, WO 1999-IE70 19990721
FDT AU 9950620 A Based on WO 200004907; EP 1098654 A1 Based on WO 200004907
PRAI IE 1998-599 19980721; IE 1998-594 19980721; IE 1998-595 19980721; IE 1998-596 19980721; IE 1998-597 19980721; IE 1998-598 19980721
IC ICM **A61K031-715**
ICS **A61K031-78; A61K031-785**
AB WO 200004907 A UPAB: 20010522
NOVELTY - Antilipemic composition comprises a biocompatible anionic **polysaccharide** material containing non **sulfated** glucuronic acid.
ACTIVITY - Antilipemic.
MECHANISM OF ACTION - None given.
USE - For lowering **cholesterol**.
ADVANTAGE - Polyanhydroglucuronic acid salts and intermolecular complexes are biocompatible, have low toxicity, no adverse side effects, and lower doses can be used compared with other antilipemic drugs.
Dwg.0/0
FS CPI
FA AB; DCN
MC CPI: A12-V01; **B04-C02**; **B04-C02A**; **B04-C02B**; **B04-C02D**; **B04-C02E3**; B04-C03B; B04-N02; B04-N04; B14-F06
TECH UPTX: 20000330
TECHNOLOGY FOCUS - POLYMERS - Preferred compounds: The polysaccharide is derived from a starch, cellulose or gum, or is of microbial origin. The polysaccharide material comprises polyanhydroglucuronic acid, its salts, copolymers or biocompatible intermolecular complex of it.
The complex comprises a complex of:

(a) an anionic component comprising a polysaccharide chain containing glucuronic acid (preferably at least 5% of the basic structural units are glucuronic acid), preferably polyanhydroglucuronic acid, its salts or copolymers, having polymeric chain containing 8-30 wt.% carboxyl groups, with at least 80% of these groups of uronic type, upto 5% carbonyl groups and upto 0.5% bound nitrogen; with molecular mass of the polymeric chain being 1x103-3x105 (preferably 5x103-1.5x105) Daltons; and
(b) a non protein cationic component comprising a natural, semi-synthetic or synthetic oligomer or polymer, preferably (i) containing nitrogen that either carries a positive charge or has a positive charge induced by contact with (a), preferably derivatives of acrylamide, methacrylamide or their copolymers, a starch, cellulose or gum, preferably guargumhydroxypropyltriammonium chloride; (ii) a synthetic or semi-synthetic polyamino acid, preferably polylysin, polyarginin or alpha,beta-poly-(N-(2-hydroxyethyl)-DL-aspartamide); (iii) a synthetic anti-fibrinolytic, preferably a hexadimethrindibromide (polybren); (iv) a natural or semi synthetic peptide, preferably protamine, gelatin or fibrinopeptide or (v) an aminoglucane derivative, preferably fractionated chitin or its de-acetylated derivative chitosan, of microbial origin or isolated from shells of arthropods e.g. crabs.

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred composition: The composition also comprises other active agents e.g. an antilipemic agent such as a phospholipid, and is in the form of a tablet, pellet, capsule, granule or microsphere.

L224 ANSWER 3 OF 9 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1998-313690 [28] WPIX
DNC C1998-096807
TI Phytosterol (ester) based **hypocholesterolaemic** agent - containing potentiating agent, e.g. tocopherol, chitosan or DNA, to accelerate serum **cholesterol** lowering effect.
DC B05
IN FABRY, B; WEITKEMPER, N
PA (HENK) HENKEL KGAA
CYC 33
PI DE 19700796 A1 19980604 (199828)* 6p A61K031-575 <--
WO 9823275 A1 19980604 (199828) DE A61K031-575 <--
RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU BR CA CN CZ HU JP KR MX NO NZ PL RU SI SK US
WO 9823277 A1 19980604 (199828) DE A61K031-70 <--
RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: AU BR CA CN CZ HU JP KR MX NO NZ PL RU SI SK US
AU 9853229 A 19980622 (199844) A61K031-575 <--
AU 9855531 A 19980622 (199844) A61K031-70 <--
DE 19700796 C2 19981112 (199849) A61K031-575 <--
NO 9902562 A 19990527 (199936) A61K000-00 <--
NO 9902564 A 19990527 (199936) A61K000-00 <--
EP 941097 A1 19990915 (199942) DE A61K031-575 <--
R: BE DE DK ES FI FR GB IT NL SE
EP 952837 A1 19991103 (199951) DE A61K031-70 <--
R: BE DE DK ES FI FR GB IT NL SE
AU 713665 B 19991209 (200009) A61K031-575 <--
AU 714993 B 20000113 (200014) A61K031-70 <--
NZ 335974 A 20000623 (200038) A61K031-355 <--
NZ 335990 A 20001027 (200062) A61K031-73 <--
JP 2001504505 W 20010403 (200126) 14p A61K031-575 <--
ADT DE 19700796 A1 DE 1997-19700796 19970113; WO 9823275 A1 WO 1997-EP6447 19971119; WO 9823277 A1 WO 1997-EP6450 19971119; AU 9853229 A AU 1998-53229 19971119; AU 9855531 A AU 1998-55531 19971119; DE 19700796 C2 DE 1997-19700796 19970113; NO 9902562 A WO 1997-EP6450 19971119, NO 1999-2562 19990527; NO 9902564 A WO 1997-EP6447 19971119, NO 1999-2564 19990527; EP 941097 A1 EP 1997-950201 19971119, WO 1997-EP6447 19971119; EP 952837 A1 EP 1997-951916 19971119, WO 1997-EP6450 19971119; AU 713665 B AU 1998-53229 19971119; AU 714993 B AU 1998-55531 19971119; NZ 335974 A NZ 1997-335974 19971119, WO 1997-EP6447 19971119; NZ 335990 A NZ 1997-335990

19971119, WO 1997-EP6450 19971119; JP 2001504505 W WO 1997-EP6447 19971119, JP 1998-524239 19971119

FDT AU 9853229 A Based on WO 9823275; AU 9855531 A Based on WO 9823277; EP 941097 A1 Based on WO 9823275; EP 952837 A1 Based on WO 9823277; AU 713665 B Previous Publ. AU 9853229, Based on WO 9823275; AU 714993 B Previous Publ. AU 9855531, Based on WO 9823277; NZ 335974 A Based on WO 9823275; NZ 335990 A Based on WO 9823277; JP 2001504505 W Based on WO 9823275

PRAI DE 1996-19649286 19961128

IC ICM **A61K000-00; A61K031-355; A61K031-575; A61K031-70; A61K031-73**

ICS **A61K031-7105; A61K031-722;** A61P003-06

ICI A61K031-575, A61K031:355; A61K031-575, A61K031:355

AB DE 19700796 A UPAB: 19980715

Use of an active agent mixture (I) for the preparation of **hypocholesterolaemic** agents, is new.

(I) comprises (A) phytosterols and/or phytosterol esters and (B) potentiating agents selected from tocopherols, chitosans, phytosterol **sulphates** and/or (deoxy)ribonucleic acids.

Also claimed is the use of gelatin for encapsulating (A) or (I).

USE - (I) is preferably administered orally in gelatin capsules, but may also be used in rectal or vaginal suppositories or dissolved or dispersed in foodstuffs.

ADVANTAGE - (B) (which themselves have no **hypocholesterolaemic** activity) potentiate and accelerate the action of (A) in reducing serum **cholesterol** levels.

Encapsulation of (I) or (A) in gelatin allows oral administration without prior art problems of taste and/or consistency.

Dwg.0/0

FS CPI

FA AB; DCN

MC CPI: B01-D02; B03-H; **B04-C02E3;** B04-E02; B04-N02; B14-F06

L224 ANSWER 4 OF 9 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD

AN 1996-039954 [04] WPIX

DNC C1996-013405

TI Compsn. contg. oligosaccharide(s) that bind to lipoprotein lipase - to prevent its interaction with receptors that would cause cellular uptake of lipoprotein, esp. to treat or prevent atherosclerosis.

DC B04

IN LARNKJR, A; OSTERGAARD, P B; LARNKJAER, A

PA (LARN-I) LARNKJAER A; (OSTE-I) OSTERGAARD P B

CYC 64

PI WO 9533468 A1 19951214 (199604)* EN 32p A61K031-725 <--

RW: AT BE CH DE DK ES FR GB GR IE IT KE LU MC MW NL OA PT SD SE SZ UG

W: AM AU BB BG BR BY CA CN CZ EE FI GE HU IS JP KE KG KP KR KZ LK LR LT LV MD MG MN MW MX NO NZ PL RO RU SD SG SI SK TJ TM TT UA UG US UZ VN

AU 9525609 A 19960104 (199613) A61K031-725 <--

ADT WO 9533468 A1 WO 1995-DK217 19950602; AU 9525609 A AU 1995-25609 19950602

FDT AU 9525609 A Based on WO 9533468

PRAI DK 1994-637 19940606

REP 03Jnl.Ref; EP 116801; EP 165569; WO 9004607

IC ICM **A61K031-725**

ICA C08B037-10

AB WO 9533468 A UPAB: 19960129

Compsn. comprises, apart from carrier or diluent, an **oligosaccharide** of formula (I):dUAp2S(1=>4)-[alpha-DGlcNp2R16R2(1=>4)-X(1=>4)]n-alpha-D-GlcNp2R16R2,where dUAp2S = 4-deoxy-alpha-L-threo-hex-4-eno-pyranosyl-uronic acid, 2-**sulphate**; alpha-D-GlcNp = alpha-D-2-deoxy-2-amino-glucopyranose; X= Idoap2R2(alpha-L-ido-pyranosyl-uronic acid) or beta-D-GlcAp (beta-D-gluco-pyranosyl-uronic acid); R1=H, **sulphate** or acetyl; R2= H or **sulphate**, and n is an integer of 3-16. (I) can bind to lipoprotein lipase (LPL) to inhibit interaction between the alpha2-macroglobulin receptor/low density lipoprotein receptor-related protein (alpha2-MR/LRP) and LPL (or its complex with lipoprotein). Such as

interaction would result in uptake of lipoprotein by mammalian cells.
USE - (I) are used to treat or prevent diseases involving interaction between alpha2-MR/LRP (esp. when expressed on smooth muscle cells or macrophages) and LPL (or its complex with lipoprotein), specifically atherosclerosis.(I) is administered at 1-100 mg/kg, given by injection, orally, nasally or rectally.
ADVANTAGE - (I) lock the anticoagulant activity of heparin.
Dwg.0/3
FS CPI
FA AB; DCN
MC CPI: **B04-C02E1; B04-C02X;** B14-F07

L224 ANSWER 5 OF 9 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1994-012195 [02] WPIX
CR 1986-103236 [16]
DNC C1994-005571
TI Blood hypolipidaemic agent with low toxicity - contains hyaluronic acid (salt) for treating menopausal disorders, sickness etc..
DC B04
PA (SEGK) SEIKAGAKU KOGYO CO LTD
CYC 1
PI JP 05320058 A 19931203 (199402)* 8p A61K031-725 <--
JP 06062425 B2 19940817 (199431) 8p A61K031-725 <--
ADT JP 05320058 A Div ex JP 1984-167775 19840813, JP 1992-322870 19840813; JP 06062425 B2 Div ex JP 1984-167775 19840813, JP 1992-322870 19840813
FDT JP 06062425 B2 Based on JP 05320058
PRAI JP 1984-167775 19840813; JP 1992-322870 19840813
IC ICM **A61K031-725**
ICS **A61K031-685; A61K037-02**
AB JP 05320058 A UPAB: 19940223
Blood hypolipidaemic agents comprise hyaluronic acid or its salts. Also claimed are agents comprising 0.01-5 pts.wt. hyaluronic acid or its salts, 1-40 pts.wt. chondroitin **sulphate**, its alkali metal salts, or alkaline earth metal salts, 0.5-20 pts.wt. lecithin, and 35-98.5 pts.wt. proteins.
Other components such as vitamins, plant extracts (e.g. Panax ginseng), amino acids, and minerals can be added. Values of total **cholesterol**, neutral lipids, and phospholiplids were lowered in blood samples in an assay using rabbits given for 60 days a feed contg. 5% a compsn. comprising 10% an aq. soln. of 1% Na hyaluronate (mol.wt. 700,000), 15% Na chondroitin **sulphate** (mol.wt. 10,000), 5% lecithin, and 79% soybean proteins.
USE/ADVANTAGE - The agents have low toxicity. The agents are used for the maintenance of physical stamina, recovery from fatigue, for improvement of unpleasant sensations in the stomach and abdominal region, menopausal disorders, sickness caused by drinking, and physical weakness, and for nourishment and toxicity. Agents contg. hyaluronic acid can also exert constipation improving activity.
Dwg.0/0
FS CPI
FA AB; DCN
MC CPI: B04-B01B; **B04-C02;** B04-N02; B05-B01P; B14-F06

L224 ANSWER 6 OF 9 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1990-012962 [02] WPIX
DNC C1990-005697
TI Physiological active polysaccharide-adsorbed lipid microspheres - useful as anti-arteriosclerotic agent.
DC B04
PA (MIZU-I) MIZUSHIMA H
CYC 1
PI JP 01294626 A 19891128 (199002)* 4p
ADT JP 01294626 A JP 1988-124796 19880520
PRAI JP 1988-124796 19880520
IC **A61K009-10; A61K031-72**
AB JP 01294626 A UPAB: 19930928

A physiological active **polysaccharide** has been adsorbed to lipid microspheres.

LM are prepd. by a known method. For example, soybean oil (10g) and egg yolk lecithin (1.2g, contg. a small amt. of phosphatidyl ethanolamine) are pre-emulsified, and glycerol (2.21g) and distilled water are added to make 10 ml in all. The blend is further emulsified and homogenised and sterilised to prepare LM. The anti-areterioslcerotic **polysaccharides** are heparin (low molecular, high molecular), sodium heparin, chondroitin **polysulphate**, heparan **sulphate**, xylan **sulphate**, **dextran sulphate** and other hepalinolides. The **polysaccharides** are adsorbed to LM are locally applied to the arteriosclerotic portion with excellent drug delivery system.

USE/ADVANTAGE - The lipid microspheres (LM) are useful as an anti-arteriosclerotic agent.

0/0

FS CPI
FA AB; DCN
MC CPI: B04-B01B; B04-B01C1; **B04-C02**; B10-E04C; **B12-H03**

L224 ANSWER 7 OF 9 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1986-198786 [31] WPIX
DNC C1986-085551
TI Anti thrombotic and lipolytic compsns. - contg. synergistic mixt. of xylan poly **sulphate** and an organic acid.
DC B03
IN BAYOL, A; BLANC, F; LANSEN, J; MAFFRAND, J P; PEREILLO, J M
PA (SNFI) SANOFI SA; (ISTS) SCLAVO SPA
CYC 12
PI FR 2574663 A 19860620 (198631)* 20p
EP 189696 A 19860806 (198632) FR
R: AT BE CH DE FR GB IT LI LU NL SE
JP 61155329 A 19860715 (198634)
ADT FR 2574663 A FR 1984-20129 19841217; EP 189696 A EP 1985-402522 19851217; JP 61155329 A JP 1985-275850 19851207
PRAI FR 1984-20129 19841217
REP 3.Jnl.Ref; EP 125152; US 3658969; US 4167562
IC **A61K031-72**
AB FR 2574663 A UPAB: 19930922
Therapeutic compsns. contg. an association of xylene **polysulphates** (I) and an organic acid (II) are new.

(I) is pref. SP 54 (also called PZ68) or a fraction isolated from this, having formula (A) where R is -SO3Na or H. This material has a mass between 1000 and 40000. It is a known material, obtd. by **sulphation** of a mixt. of xylanes extracted from beech wood. The acid (II) is pref. di- or poly-carboxylic, esp. citric, isocitric, tartaric, malic or ascorbic acids. The compsns. may be given orally, parenterally, rectally or locally, the unit dose of (I) being 0.030 g - 0.250 g and that of (II) being 0.050-0.250 g. The daily dose of (I) is 0.030g - 1.00 g.

USE/ADVANTAGE - Antithrombotic and lipolytic agents. The association of (I) with (II) has a synergistic effect.

0/0

FS CPI
FA AB
MC CPI: B03-F; **B04-C02D**; B10-C02; B12-C09; B12-H02; **B12-H03**

L224 ANSWER 8 OF 9 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1979-69822B [38] WPIX
TI Intravenous soln. for treating arteriosclerosis - comprising Ringers solution and at least eleven added ingredients.
DC B05
PA (EVER-I) EVERS H R
CYC 5
PI US 4167562 A 19790911 (197938)*
DE 2934718 A 19800313 (198012)

GB 2029218 A 19800319 (198012)
FR 2434620 A 19800430 (198024)
GB 2029218 B 19830126 (198304)
IL 58017 A 19830515 (198329)
PRAI US 1978-937533 19780828
IC **A61K009-08; A61K031-72; A61K033-14; A61K037-40**
AB US 4167562 A UPAB: 19930901
An intravenous soln. for the treatment of arteriosclerosis consists of the following per 10 ml. of standard Ringers soln.: (a) B-complex, 1,000-5,000 mg.; (b) hydrochloric acid U.S.P., 10-40 mg.; (c) sodium ascorbate, 500-25,000 mg.; (d) pyridoxine hydrochloride, 500-5,000 mg.; (e) magnesium **sulphate**, 100-2,500 mg.; (f) adrenal cortex, 250-2,500 mcg.; (g) magnesium chloride, 250-5000 mg.; (h) thiamin, 100-2,000 mg.; (i) heparin sodium, 2,500-25,000 U.S.P. units; (j) calcium gluconate, 250-2,500 mg.; and (k) calcium d-saccharate, 1.6-5.0 mg.
Ringers soln. normally contains, per 10 ml., NaCl, 86 mg.; KCl, 3 mg.; and CaCl2, 3.3. mg.
FS CPI
FA AB
MC CPI: B03-L; B04-B04G; **B04-C02**; B05-A01B; B05-C07; B07-D04; B10-A07; B10-A22; B10-B02D; B10-D03; B12-E01; B12-F01; **B12-H03**; B12-M07

L224 ANSWER 9 OF 9 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1973-64575U [43] WPIX
TI Oligosaccharide sulphuric acid ester - for treatment of arteriosclerosis.
DC B04
PA (CHUG) CHUGAI PHARMACEUTICAL CO
CYC 4
PI JP 48048618 A (197343)*
DE 2319774 A 19741031 (197445)
GB 1381426 A 19750122 (197504)
FR 2226162 A 19741220 (197507)
PRAI JP 1971-82854 19711021
IC **A61K027-00; A61K031-72**; C08B027-00
AB JP 48048618 A UPAB: 19930831
Title ester is effectively absorbed by the gastrointestinal tract when administered orally in combination with a non-ionic surface active agent. In an example 100 mg **oligosaccharide sulphate** (ave. glucose unit 8, S content 5%) in which glucose is linked in 6-membered and 10 mg polyoxyethylene lauryl alcohol ether were dissolved in 5 ml water, and the soln. was orally administered to a rat. The rate of urinary excretion of the **oligosaccharide sulphate** was 3.0% whereas that in controls receiving only **oligosaccharide sulphate** alone was 0.3%.
FS CPI
FA AB
MC CPI: **B04-C02**; B04-C03; **B12-H03**

=> d all abeq tech tot

L232 ANSWER 1 OF 8 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1999-527033 [44] WPIX
DNC C1999-154779
TI Preparation of 4-(6-(hexylcarbamoyloxy)hexylcarbamoyloxy)-piperidine-1-carboxylic acid 4-phenoxyphenyl ester comprises carbonylation and coupling reaction, then carbonylation/hexylamine reaction, dealkylation and phenoxycarbonylation.
DC B03
IN JIRKOVSKY, I
PA (AMHP) AMERICAN HOME PROD CORP
CYC 1
PI US 5952506 A 19990914 (199944)* 7p C07D211-46
ADT US 5952506 A Provisional US 1997-44805 19970424, US 1998-62515 19980417

PRAI US 1997-44805 19970424; US 1998-62515 19980417
IC ICM C07D211-46
AB US 5952506 A UPAB: 19991026
NOVELTY - Preparation of 4-(6-(hexylcarbamoyloxy)hexylcarbamoyloxy)-piperidine-1-carboxylic acid 4-phenoxyphenyl ester comprises reacting 1-benzyl- (or 1-methyl-) 4-hydroxypiperidine with carbonylating agent and 6-aminohexanol, followed by reaction with a carbonylating agent and hexylamine, followed by dealkylation and concomitant phenoxycarbonylation.

DETAILED DESCRIPTION - Preparation of 4-(6-(hexylcarbamoyloxy)hexylcarbamoyloxy)-piperidine-1-carboxylic acid 4-phenoxyphenyl ester (I) comprises:

(a) reacting 1-benzyl-4-hydroxypiperidine or 1-methyl-4-hydroxypiperidine in an aprotic solvent at 0-70 deg. C (optionally in the presence of a tertiary amine) with:

(i) a carbonylating coupling reagent selected from carbonyldiimidazole, disuccinimidyl carbonate, 2,2'-carbonyl-bis(3,5-dioxo-1,2,4-oxazolidine) or 3,3'-carbonyl bis(5-phenyl-1,3-1,3,4-oxadiazole-2(3H)thione) and;

(ii) 6-aminohexanol;

(b) reacting the resultant 4-((6-hydroxyhexyl)carbamoyloxy)piperidine derivative in an aprotic solvent at 0-70 deg. C (optionally in the presence of a tertiary amine) with:

(i) a carbonylating coupling reagent as above; and

(ii) hexylamine; and

(c) dealkylation and concomitant N-(4-phenoxy)phenoxycarbonylation of the intermediate 4-(6-(hexylcarbamoyloxy)hexylcarbamoyloxy)piperidine derivative with 4-phenoxyphenyl chloroformate in an aprotic solvent at 15-110 deg. C to give (I).

ACTIVITY - Antilipemic; antiarteriosclerotic.

MECHANISM OF ACTION - **Sterol-Esterase**-Inhibitor; **Sterol-O-Acyltransferase**-Inhibitor; **ACAT**-Inhibitor.

USE - For the large-scale preparation of (I) (claimed). (I) is useful for reducing **cholesterol** absorption and in the treatment of **hypercholesterolemia**, hyperlipidemia and atherosclerosis.

ADVANTAGE - (I) inhibits **cholesterol ester hydrolase** and acylcoenzyme A **cholesterol acyltransferase**. The preparation is carried out without isolation of intermediates and without changing solvents. The preparation gives improved purity, higher yields, lower costs, technical convenience and is less labor and time intensive than the prior art route in EP0635501-A1.

Dwg.0/0
FS CPI
FA AB; GI; DCN
MC CPI: B07-D05; B11-C01; **B14-D02A2**; B14-D06; B14-D07A; B14-F06; B14-F07
TECH UPTX: 19991026
TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Preparation: The carbonylating coupling reagent is carbonyldiimidazole, the reactions are carried out in the presence of triethylamine and the aprotic solvent is toluene.

The intermediate from step (a) is either 1-benzyl-4-((6-hydroxyhexyl)carbamoyloxy)piperidine or 1-methyl-4-((6-hydroxyhexyl)carbamoyloxy)piperidine. The intermediate from step (b) is either 1-benzyl-4-((6-hexylcarbamoyloxy)hexylcarbamoyloxy)piperidine or 1-methyl-4-((6-hexylcarbamoyloxy)hexylcarbamoyloxy)piperidine. Step (c) is claimed per se.

L232 ANSWER 2 OF 8 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1999-243579 [20] WPIX
DNN N1999-181297 DNC C1999-070962
TI Reducing mammalian serum total **cholesterol** for treating hyperlipidemia, **hypercholesterolemia** and atherosclerosis.
DC B04 D13 D16 P14
IN CHERUKURI, R S V; CHERUVANKY, R; LYNCH, I E; MCPEAK, P
PA (RICE-N) RICEX CO INC; (RICE-N) RICEX CO

CYC 82
PI WO 9911144 A1 19990311 (199920)* EN 40p A23K001-00
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
AU 9892098 A 19990322 (199931) A23K001-00
US 6126943 A 20001003 (200050) A61K035-78
ADT WO 9911144 A1 WO 1998-US17881 19980828; AU 9892098 A AU 1998-92098 19980828; US 6126943 A Provisional US 1997-57870 19970902, US 1998-143159 19980828
FDT AU 9892098 A Based on WO 9911144
PRAI US 1997-57870 19970902; US 1998-143159 19980828
IC ICM A23K001-00; A61K035-78
ICS A01K029-00; A01N065-00; C12P001-00
AB WO 9911144 A UPAB: 19990525
NOVELTY - Reducing mammalian serum total **cholesterol**, low density lipoprotein (LDL) **cholesterol**, apolipoprotein B and triglyceride levels, comprises ingesting a stabilized rice bran derivative obtained by enzyme treatment of rice bran, and/or an insolubilized fraction.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) preparing enzyme treated stabilized rice bran derivative comprising:

(a) mixing stabilized rice bran with an aqueous solution to form a 15-35% sold rice bran slurry;

(b) adding an enzyme to the slurry to convert starch to dextrin; and

(c) drying the slurry to obtain the stabilized rice bran derivative;

(2) the product of the preparation of (1); and

(3) a method for increasing the high density lipoprotein (HDL)/LDL **cholesterol** ratio in mammalian serum, comprising ingesting a stabilized rice bran derivative obtained by enzyme treatment of rice bran, and/or an insolubilized fraction.

ACTIVITY - Antiarteriosclerotic; Antilipemic.

MECHANISM OF ACTION - The major bioactive components present in the rice bran derivatives are tocopherols, tocotrienols, gamma -oryzanol, phytosterols, polyphenols, inositol, B vitamins, protein, fiber, and fat. The components act mostly synergistically, e.g. by enzyme inhibitions: three enzymes, namely 3-hydroxy-3-methylglutaryl-coenzyme A (HMGCoA) reductase, Acyl coenzyme A transferase (**ACAT**) and esterase are inhibited. HMGCoA reductase, a key enzyme involved in the **cholesterol** biosynthesis is inhibited by the tocotrienols, post transcriptionally, reducing the synthesis of **cholesterol** resulting in low circulating **cholesterol**. Acyl coenzyme A transferase (**ACAT**), inhibition is brought about by:

(a) the prevention of cellular **cholesterol** esterification thereby enriching high density lipoprotein **cholesterol** (HDL) with free **cholesterol**;

(b) elevation of HDL, a positive effect, and decreased synthesis of very low density lipoprotein **cholesterol** (VLDL); and

(c) increased clearance of **cholesterol** as bile acids and bile salts.

The net result is lower circulating **cholesterol**. **Cholesterol esterases** are inhibited by cycloartenol, a component of -y-oryzanol, resulting in a slower hydrolysis of **cholesterol** esters and decreased absorption. This results in lower circulating total **cholesterol**. gamma -Oryzanol inhibits platelet aggregation, and aortic streaks thus reducing atherosclerosis. Rice bran derivatives contain a significant variety and concentration of antioxidants. Antioxidants such as tocopherols, tocotrienols, gamma -oryzanol, polyphenols as ferulic acid, and lipoic acid are involved in the repair of free radical damage, preventing low density lipoprotein **cholesterol** (LDL) oxidation, resulting in the reduction of vascular damage that can lead to cardiovascular disease. Cycloartenol, a

component of gamma -oryzanol, has a structure similar to **cholesterol** and competes with receptor sites of **cholesterol**. This causes a sequestration of **cholesterol** as bile salts and bile pigments, thus maintaining lower levels of circulating **cholesterol**. Phytosterols and fiber facilitate **cholesterol** sequestration from the body through increased excretion of bile salts and bile acids, resulting in lower levels of circulating **cholesterol**. The protein, fat (with high levels of polyunsaturated and monounsaturated fatty acids), and B vitamins also contribute to the **hypocholesterolemic** effect.

USE - The method is used to treat subjects in which elevated levels of serum total **cholesterol**, LDL-**cholesterol**, VLDL-**cholesterol**, apolipoprotein B and triglyceride levels may lead to hyperlipidemia, cardiovascular disease, atherosclerosis, arteriosclerosis or xanthomatosis.

Dwg.0/0

FS CPI GMPI
FA AB; DCN
MC CPI: B04-A10G; **B14-D02A2**; B14-F01; B14-F06; B14-F07; D03-H01T1; D03-H01T2; D03-L; D05-A01A4; D05-A01B
TECH UPTX: 19990517

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred materials: The rice bran derivative comprises 40-60 %w/w dietary fiber. The derivative is an insolubilized fraction comprising (w/w): 1-10% total non-fiber carbohydrate content; 10-20% total fat content; and 15-25% total protein.

TECHNOLOGY FOCUS - FOOD - Preferred materials: The rice bran derivative comprises 40-60 %w/w dietary fiber. The derivative is an insolubilized fraction comprising (w/w): 1-10% total non-fiber carbohydrate content; 10-20% total fat content; and 15-25% total protein.
Preferred method: The aqueous slurry is heated to 100-200 (especially 150-200)degreesF using a steam injection cooker or a heat exchanger, after the enzyme (especially dextranase, a maltase or an alpha-amylase) has been added. The drying is carried out using belt drying, spray drying, drum drying or air drying.

L232 ANSWER 3 OF 8 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1998-609956 [51] WPIX
DNC C1998-182788
TI 4-Carbamoyloxy-piperidine-1-carboxylate ester derivative preparation - in 3 stages from 4-hydroxy-piperidine derivative via new intermediates, used as **cholesterol** absorption inhibitor.
DC B03 B05
IN JIRKOVSKY, I
PA (AMHP) AMERICAN HOME PROD CORP
CYC 79
PI WO 9847870 A1 19981029 (199851)* EN 14p C07D211-46
RW: AT BE CH DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW
AU 9869469 A 19981113 (199913) C07D211-46
ZA 9803399 A 19991229 (200006) 16p C07D000-00
ADT WO 9847870 A1 WO 1998-US6513 19980331; AU 9869469 A AU 1998-69469 19980331; ZA 9803399 A ZA 1998-3399 19980422
FDT AU 9869469 A Based on WO 9847870
PRAI US 1997-845565 19970424
IC ICM C07D000-00; C07D211-46
ICS C07C068-02; C07C069-96
AB WO 9847870 A UPAB: 19981223
Preparation of 4-[(6-hexylcarbamoyloxy)- hexylcarbamoyl]piperidine-1-carboxylic acid 4-phenoxyphenyl ester (I) comprises: (a) reacting 1-(benzyl or methyl)-4-hydroxypiperidine (II) with a carbonylating coupling reagent and 6-aminohexanol (III) in an aprotic solvent at 0-70

deg. C, optionally in the presence of a tertiary amine; (b) reacting the resultant 1-(benzyl or methyl)-4-[(6-hydroxyhexyl)carbamoyloxy]-piperidine (IV) with hexylamine (V) under the conditions of step (1); and (c) dealkylation and concomitant N-(4-phenoxy)-phenoxycarbonylation of the intermediate 1-(benzyl or methyl)-4-[6-(hexylcarbamoyloxy)-hexylcarbamoyloxy]piperidine (VI) with 4-phenoxyphenyl chloroformate (VII) in an aprotic solvent 15-110 deg. C. Also claimed are novel intermediates (IV), (VI) and (VII). Step (c) is also claimed as a separate process.

USE - (I), described in EP 635501, inhibits both **cholesterol ester hydrolase** and acyl-coenzyme A **cholesterol acyltransferase**, resulting in a reduction of **cholesterol** absorption. Possible uses include treatment of **hypercholesterolaemia**, hyperlipidaemia and atherosclerosis.

ADVANTAGE - This method utilises a single solvent throughout, requires no purification of intermediates and is suitable for large-scale production. The yield and purity of (I) are higher than in the normal laboratory-scale synthesis and the method is much less labour intensive.

Dwg.0/0

FS CPI
FA AB; DCN
MC CPI: B07-D05; B14-F06; B14-F07

L232 ANSWER 4 OF 8 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1995-053622 [08] WPIX
DNC C1995-024413
TI New tris carbamic acid ester(s) are **ACAT** inhibitors - useful for treating e.g. atherosclerosis, familial **hypercholesterolaemia** and hyperlipaemia.
DC B03
IN COMMONS, T J; LACLAIR, C M; STRIKE, D P; COMMONS, T J W
PA (AMHP) AMERICAN HOME PROD CORP
CYC 29
PI

EP 635501	A1	19950125 (199508)*	EN 35p		C07D295-215
R: AT BE CH DE DK ES FR GB GR IE IT LI LU NL PT SE					
AU 9467520	A	19950202 (199513)			C07D211-46
CA 2128116	A	19950122 (199516)			C07D211-46
FI 9403441	A	19950122 (199516)			C07D211-46
BR 9402852	A	19950404 (199520)			C07D207-16
JP 07089934	A	19950404 (199522)	27p		C07D211-46
NZ 264032	A	19951221 (199606)			C07D211-04
ZA 9405214	A	19960327 (199619)	55p		C07D000-00
HU 70942	T	19951128 (199733)			C07D211-46
BR 1100752	A3	19980505 (199825)			C07D401-12
SG 47596	A1	19980417 (199826)			C07D295-215
IL 110302	A	19980615 (199836)			C07D205-04
AU 692157	B	19980604 (199839)			C07D211-46
HU 216790	B	19990830 (199940)			C07D211-46
US 5952354	A	19990914 (199944)			A61K031-445
RU 2130928	C1	19990527 (200027)			C07D211-16
TW 369527	A	19990911 (200035)#			C07D211-06

ADT EP 635501 A1 EP 1994-305305 19940719; AU 9467520 A AU 1994-67520 19940718; CA 2128116 A CA 1994-2128116 19940715; FI 9403441 A FI 1994-3441 19940720; BR 9402852 A BR 1994-2852 19940718; JP 07089934 A JP 1994-165075 19940718; NZ 264032 A NZ 1994-264032 19940718; ZA 9405214 A ZA 1994-5214 19940715; HU 70942 T HU 1994-2108 19940715; BR 1100752 A3 BR 1997-1100752 19970512; SG 47596 A1 SG 1996-3025 19940719; IL 110302 A IL 1994-110302 19940713; AU 692157 B AU 1994-67520 19940718; HU 216790 B HU 1994-2108 19940715; US 5952354 A US 1993-95140 19930721; RU 2130928 C1 RU 1994-26296 19940715; TW 369527 A TW 1994-100154 19940110
FDT AU 692157 B Previous Publ. AU 9467520; HU 216790 B Previous Publ. HU 70942
PRAI US 1993-95140 19930721; TW 1994-100154 19940110
REP 01Jnl.Ref; EP 428385; EP 431321; US 5112859; WO 9313067
IC ICM A61K031-445; C07D000-00; C07D205-04; C07D207-16; C07D211-04; C07D211-06; C07D211-16; C07D211-46; C07D295-215; C07D401-12
ICS A61K031-395; A61K031-40; A61K031-415; A61K031-425; A61K031-435; A61K031-44; A61K031-47; A61K031-495; A61K031-505; A61K031-535;

A61K031-54; A61K031-55; C07D207-10; C07D207-12; C07D211-36; C07D211-44; C07D211-62; C07D223-06; C07D223-08; C07D225-02; C07D295-092; C07D401-14; C07D403-06; C07D403-12; C07D403-14; C07D405-00; C07D405-12; C07D405-14; C07D409-06; C07D409-12; C07D409-14; C07D409-60; C07D413-00; C07D413-12; C07D413-14; C07D417-00; C07D417-12; C07D417-14; C12N009-99

ICI C07D211:46, C07D221:20, C07D401-12; C07D211:46, C07D221:20, C07D307:91, C07D405-14

AB EP 635501 A UPAB: 19950602

Tris carbamic acid esters of 4 - 8 membered azacycloalkanols of formula (I) and their salts are new; p = 0 - 4, Z = -Ar1, -Ar1-Ar2-, -Ar1-O-Ar2, -Ar1-S-Ar2, -Ar1-O-C(O)-Ar2, -Ar1-C(O)-O-Ar2, -Ar1-C(O)-Ar2, -Ar1-(CH2)1-20-Ar2, -Ar1-(CH2)1-20-O-Ar2, -Ar1-O-(CH2)1-20-Ar2, -Ar1-(CR6=CR6)1-3-Ar2, -(CR6=CR6)1-3-Ar2 or -Ar1-NR7-Ar2; R6 = H or 1-8C alkyl; R7 = H, 1-8C alkyl, 1-8C alkylcarbonyl or 1-8C alkoxycarbonyl; Ar1, Ar2 = Ph, naphthyl, furanyl, benzofuranyl, pyrazinyl, thienyl, benzothienyl, imidazolyl, benzoxazolyl, thiazolyl, benzthiazolyl, indenyl, indolyl, quinolinyl, benzotriazolyl, carbazolyl, benzimidazolyl or fluorenyl etc. (all opt. substd.); A = a bridging gp. selected from 1-20C hydrocarbyl opt. unsatd. with 1-6 sites of olefinic and/or acetylenic unsaturation, -(CH2)m-W-(CH2)n- or -(CH2)b-Y-(CH2)c-; m, n = 1 - 19; m + n = 2 - 20; W = -O-, -S- or NR14; R14 = H, 1-20C alkyl, 1-20C alkylcarbonyl, 1-20C alkoxycarbonyl or benzyl; b, c = 0 - 20; b + c = 1 - 20, Y = phenylene, pyridinylene, naphthylene, pyrrolylene or a gp. of formula (ii) - (v) etc.; R15 = H, 1-8C alkyl, 1-20C alkylcarbonyl, 1-20C alkoxycarbonyl or benzyl; R1, R2 = H, 1-8C alkyl, 1-8C alkoxy, 1-8C alkylcarbonyl, OH, CN, 1-8C alkylcarbonyloxy or -(CH2)0-6-NR18R19; R18 = 1-8C alkyl, 1-8C alkoxycarbonyl or 1-8C alkylcarbonyl; R19 = H or 1-8C alkyl; R3 = H, 1-8C alkyl or 7-15C arylalkyl; aryl = Ph opt. substd. by 1-6C alkyl; R4, R5 = H, 1-20C alkyl, 2-20C alkenyl, 3-10C cycloalkyl, -(CH2)1-20-(3-10C cycloalkyl), -(CH2)1-20-Ar1 or -(CH2)1-20NR20R21; R20 = 1-20C alkyl, 2-20C alkenyl, 1-20C alkylcarbonyl, 1-20C alkoxycarbonyl or benzyl; R21 = H or 1-20C alkyl;

USE - (I) inhibit absorption of **cholesterol** from the intestinal tract and inhibit enzymes **cholesterol ester hydrolase** (CEH) and **acyl-CoA cholesterol acyltransferase** (**ACAT**). (I) are useful for treating atherosclerosis, familial **hypercholesterolaemia** and hyperlipidaemia.

Dwg.0/0

FS CPI

FA AB; GI; DCN

MC CPI: B06-H; B07-D03; B07-H01; **B14-D02A2**; B14-D06; B14-D07A; B14-F06; B14-F07

L232 ANSWER 5 OF 8 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD

AN 1992-432990 [52] WPIX

DNC C1992-192232

TI New 1-piperidine carboxylic acid 4-phenoxyphenyl ester derivs. - are CEH and **ACAT** inhibitors for treating **hypercholesterolaemia**, hyperlipaemia, coronary heart disease and atherosclerosis.

DC B03

IN COMMONS, T J; STRIKE, D P

PA (AMHP) AMERICAN HOME PROD CORP

CYC 39

PI US 5169844 A 19921208 (199252)* 10p A61K031-445

WO 9313067 A1 19930708 (199328) EN 28p C07D211-46

RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL OA PT SE

W: AU BB BG BR CA CS FI HU JP KP KR LK MG MN MW NO NZ PL RO RU SD

AU 9334251 A 19930728 (199347) C07D211-46

ADT US 5169844 A US 1991-812512 19911220; WO 9313067 A1 WO 1992-US11287 19921210; AU 9334251 A AU 1993-34251 19921210

FDT AU 9334251 A Based on WO 9313067

PRAI US 1991-812512 19911220

REP 2.Jnl.Ref; EP 428385; US 5112859

IC ICM A61K031-445; C07D211-46

ICS A61K031-435; A61K031-495; A61K031-54; C07D401-12; C07D417-12
AB US 5169844 A UPAB: 19931118
Phenoxyphenyl 1-piperidinecarboxylate derivs. of formula (I) are new. In (I) R1 = H, 1-20C alkyl, 3-20C alkenyl, 3-8C cycloalkyl, 3-8C cycloalkyl-(1-6C)alkyl, phenyl (opt. substd. by 1-6C alkyl, 1-6C alkoxy, halo, NO2, CN or CF3) or phenyl-(1-20C) alkyl (opt. ring substd. by 1-6C alkyl, 1-6C alkoxy, halo, NO2, CN, CF3 or Ph); R2 = H or 1-6C alkyl; or NR1R2 forms a gp. of formula (a): n = 0-2; X = O, S or CR7R8; R7 = H, OH, 1-6C alkyl, 2-6C alkanoyloxy, 1-6C hydroxyalkyl, COOH, 1-16C alkoxycarbonyl(sic) or phenyl (opt. substd. by 1-6C alkyl, 1-6C haloalkyl, 1-6C perhaloalkyl, halo, NO2 or CN); R8 = H or 1-6C alkyl; or R7+R8 completes a 3-7C polymethylene ring; R9 = H, 1-6C alkyl or 2-12C gem dialkyl; R3-R6 = H, 1-6C alkyl, 1-6C alkoxy, halo, NO2, CN, 1-6C perhaloalkyl, 1-16C alkoxycarbonyl(sic) or COOH.
USE - (I) inhibit **cholesterol** ester hydrolose (CEH) and/or acyl coenzyme A:**cholesterol acyltransferase** (**ACAT**) and so inhibit the formation of **cholesteryl** esters. Thus (I) interfere with, and prevent, assimilation of **cholesterol** into the lymphotic system and thus the bloodstream. (I) can be used to treat high serum **cholesterol** levels and associated diseases (e.g, coronery heart disease, atherosclerosis, familiar **hypercholesterolaemia** and hyperlipaemia).
0/0
Dwg.0/0
FS CPI
FA AB; GI; DCN
MC CPI: B07-D05; B12-F02; B12-G01B2; B12-G01B3; **B12-H03**
ABEQ WO 9313067 A UPAB: 19931116
Phenoxyphenyl 1-piperidinecarboxylate derivs. of formula (I) are new. In (I), R1 = H, 1-20C alkyl, 3-20C alkenyl, 3-8C cycloalkyl, 3-8C cycloalkyl-(1-6C)alkyl, phenyl (opt. substd. by 1-6C alkyl, 1-6C alkoxy, halo, NO2, CN or CF3) or phenyl-(1-20C) alkyl (opt. ring substd. by 1-6C alkyl, 1-6C alkoxy, halo, NO2, CN, CF3 or Ph); R2 = H or 1-6C alkyl; or NR1R2 forms a gp. of formula (a); n = 0-2; X = O, S or CR7R8; R7 = H, OH, 1-06C alkyl, 2-6C alkanoyloxy, 1-6C hyroxyalkyl, COOH, 1-16C alkoxycargbonyl (sic) or phenyl (opt. substd. by 1-6C alkyl, 1-6C haloalkyl, 1-6C perhaloalkyl, halo, NO2 or CN); R8 - HG or 1-6C alkyl; or R7+R8 completes a 3-7C polymethylene ring; R9 = H, 1-6C alkyl or 2-12C gem dialkyl; R3-R6 = H, 1-6C alkyl, 1-6C alkoxy, halo, NO2, CN, 1-6C perhaloalkyl, 1-16C alkoxycarbonyl (sic) or COOH.
USE - (I) inhibit **cholesterol** ester hydrolose (CEH) and/or acyl coenzyme A:**cholesterol acyltransferase** (**ACAT**) and so inhibit the formation of **cholesteryl** esters. Thus (I) interferes with, and prevent, assimilation of **cholesterol** into the lymphotic system and thus the bloodstream. (I) can be used to treat high serum **cholesterol** levels and associated diseases (e.g. coronery heart disease, atherosclerosis, familiar **hypercholesterolaemia** and hyperlipaemia).
Dwg. 0/0

L232 ANSWER 6 OF 8 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1992-133595 [17] WPIX
DNC C1992-062469
TI New tri cyclic heterocyclic derivs. are **ACAT** inhibitors - used for treating **hypercholesterolaemia**, atherosclerosis, myocardial infarction etc..
DC B02
IN IKEDA, H; MEGURO, K; TAWADA, H
PA (TAKE) TAKEDA CHEM IND LTD
CYC 17
PI EP 481243 A 19920422 (199217)* EN 34p
R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE
CA 2052287 A 19920328 (199223) C07D221-06
JP 05009179 A 19930119 (199311) 21p C07D221-06
US 5264454 A 19931123 (199348) 19p C07D311-92
US 5418239 A 19950523 (199526) 18p A61K031-44

ADT EP 481243 A EP 1991-116099 19910921; CA 2052287 A CA 1991-2052287 19910926; JP 05009179 A JP 1991-202003 19910812; US 5264454 A US 1991-765182 19910925; US 5418239 A Div ex US 1991-765182 19910925, US 1993-117950 19930908
FDT US 5418239 A Div ex US 5264454
PRAI JP 1990-259657 19900927; JP 1991-202003 19910812
REP EP 354994
IC ICM A61K031-44; C07D221-06; C07D311-92
ICS A61K031-35; A61K031-365; A61K031-435; A61K031-47; C07D221-16; C07D311-78; C07D311-94
AB EP 481243 A UPAB: 19931006
Fused heterocycle derivs. of formula (I) and their salts are new. Ring A and ring B= opt. substd. benzene; X= N(O)m= C(R2), N(R3)-CO or O-CO; R2= H, alkyl or alkoxy; m= 0-1; R3= H or alkyl; Y= bond, NH, 1-2C alkylene or vinylene; R1= opt. substd. hydrocarbyl; n= 3-6. Ring A and ring B= benzene opt. substd. by 1-4 of halo, 1-6C alkyl (opt. substd. by halo), 1-6C alkoxy (opt. substd. by halo), 1-6C alkylthio (opt. substd. by halo), 1-3C acyloxy, di(1-6C alkyl); amino or OH (esp. A=benzene substd. by 1-3 of halo, 1-6C alkyl or OH and B= benzene). X= N= CR2, NR3CO or OCO, R2= H or 1-6C alkoxy; R3= 1-6C alkyl; Y= NH or 1-2C alkylene; R1= 1-8C alkyl, 3-7C cycloalkyl, 3-7C cycloalkyl-(1-4C) alkyl, 6-10C aryl or 7-16C aralkyl all opt. substd. by 1-5 of halo, 1-6C alkyl (opt. substd. by halo), 1-6C alkoxy, (opt. substd. by halo), 1-6C alkylthio (opt. substd. by halo), 1-3C acyloxy, di(1-6C alkyl) amino or OH (esp. phenyl substd. by 1-3 of halo, 1-6C alkyl, 1-6C alkoxy, 1-6C acyloxy (sic), di(1-6C alkyl)amino or H (partic. 2,4-difluorophenyl)). n=3.
USE - (I) are **acyl-CoA:cholesterol acyl transferase** (**ACAT**) inhibitors
ACAT inhibitors inhibit the absorption of dietary **cholesterol** from the intestinal tract, suppress the increase in **cholesterol** levels in the blood and suppress the accumulator of intracellular **cholesterol**. (I) are useful for treating **hypercholesterolaemia** and atherosclerosis and diseases associated with them e.g. ischaemic heart disease such as myocardial infarction and cerebrovascular disorders such as cerebral infarction and cerebral apoplexy). (0/0)
0/0
FS CPI
FA AB; GI; DCN
MC CPI: B06-H; B12-F01B; B12-F02; B12-G01B2; **B12-H03**
ABEQ US 5264454 A UPAB: 19940120
Heterocyclic derivs. of formula (I) and their salts are new; in which benzene rings A and B are opt. substd. by 1-4 of halo, opt. halogenated 1-6C alkyl, opt. halogenated 1-6C alkoxy, opt. halogenated 1-6C alkylthio, 1-3C acyloxy, di-(1-6C alkyl)amino and OH; X is -O-CO-; Y is a bond, NH or CHCH; R1 is 1-8C alkyl, 3-7C cycloalkyl, (3-7C cycloalkyl)-(1-4C alkyl), 1-6C aryl or 7-6C aralkyl opt. substd. by 1-5 of halo, opt. halogenated (1-6C alkyl, 1-6C alkoxy or 1-6C alkylthio), 1-3C acyloxy, di-(1-6C alkyl)amino and OH; n is 3, 4, 5, 6.
(I) is specifically N-(2,4-difluorophenyl)- N'(4-(2-methylphenyl)-2-oxo-2,6,7,8- tetrahydrocyclopenta (g)(1)benzo- pyran-3-yl) urea.
USE/ADVANTAGE - (I) are **acyl-CoA: cholesterol acyltransferase** inhibitors useful for prevention and treatment of **hypercholesterolemia**, atherosclerosis, ischaemic heart diseases, including myocardial infarction, and cerebrovascular disorders, including cerebral infarction and cerebral apoplexy.
Dwg. 0/0
ABEQ US 5418239 A UPAB: 19950705
Heterocyclic cpds. of formula (I) and their salts are new: where n is 3-6; benzene rings A and B are opt. substd. by 1-4 of:1 halogen, or 1-6C alkyl, 1-6C alkoxy or 1-6C alkylthio, each opt. halogenated, or 1-3C acyloxy, di-(1-6C alkyl)amino or OH; X is -N(O)m=C(R2)- (in which m is 0 or 1; R2 is H, alkyl or alkoxy), or is -N(R3)-CO- (in which R3 is H or alkyl); Y is a bond, -NH-, 1 or 2C alkylene or -CH=CH-; R1 is 1-8C alkyl, 3-7C cycloalkyl, 3-7C cycloalkyl(1-4C alkyl), 6-10C aryl or 7-16C aralkyl, each

opt. substd. by 1-5 of the substits. as for A and B.
N-(4-(2-Chlorophenyl)- 7,8-dihydro-6H-cyclopenta (g)quinolin-3-yl)-N'-(2,4-difluorophenyl)urea is specifically claimed.
USE - Acyl-CoA:**cholesterase** acyltransferase (**ACAT**) inhibitor comprises comprising a cpd. (I) and a carrier are claimed, and can be given to a mammal to treat **hypercholesterolaemia**, atherosclerosis, heart diseases and cerebrovascular disorders.
Dwg.0/0

L232 ANSWER 7 OF 8 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1990-348258 [46] WPIX
CR 1991-178095 [24]; 1996-087083 [09]
DNC C1990-151144
TI Inhibition of intestinal **cholesterol** absorption - by oral admin of non-absorbable inhibitor of **cholesterol esterase**, esp. high mol.wt. **sulphated polysaccharide**.
DC B04 D16
IN LANGE, L G; SPILBURG, C A
PA (LANG-I) LANGE L G; (SPIL-I) SPILBURG C A; (SCHI-I) SCHIERANO P
CYC 17
PI WO 9012579 A 19901101 (199046)* 49p
RW: AT BE CH DE DK ES FR GB IT LU NL SE
W: AU CA JP US
AU 9055356 A 19901116 (199107)
US 5017565 A 19910521 (199123) 8p
US 5063210 A 19911105 (199147) 11p
EP 469079 A 19920205 (199206)
R: AT BE CH DE ES FR GB IT LI LU NL SE
JP 04503813 W 19920709 (199234) 19p A61K045-00 <--
AU 633569 B 19930204 (199312) A61K031-715 <--
EP 469079 B1 19941207 (199502) EN 29p A61K031-72 <--
R: AT BE CH DE DK ES FR GB IT LI LU NL SE
DE 69014870 E 19950119 (199508) A61K031-72 <--
ES 2064736 T3 19950201 (199511) A61K031-72 <--
JP 08019001 B2 19960228 (199613) 19p A61K045-00 <--
US 5616570 A 19970401 (199719)# 20p A61K031-72 <--
CA 2053258 C 19980210 (199817) A61K031-72 <--
US 5792832 A 19980811 (199839) C07K007-06
ADT US 5017565 A US 1989-340868 19890420; US 5063210 A US 1989-429398 19891031; EP 469079 A EP 1990-907923 19900420; JP 04503813 W JP 1990-506819 19900420, WO 1990-US2079 19900420; AU 633569 B AU 1990-55356 19900420; EP 469079 B1 EP 1990-907923 19900420, WO 1990-US2079 19900420; DE 69014870 E DE 1990-614870 19900420, EP 1990-907923 19900420, WO 1990-US2079 19900420; ES 2064736 T3 EP 1990-907923 19900420; JP 08019001 B2 JP 1990-506819 19900420, WO 1990-US2079 19900420; US 5616570 A Cont of WO 1990-US2079 19900420, Cont of US 1991-773875 19911018, US 1994-283723 19940801; CA 2053258 C CA 1990-2053258 19900420; US 5792832 A Cont of US 1989-429398 19891031, Cont of US 1989-434899 19891113, Cont of US 1992-856910 19920512, Div ex US 1994-350801 19941207, US 1995-461881 19950605
FDT JP 04503813 W Based on WO 9012579; AU 633569 B Previous Publ. AU 9055356, Based on WO 9012579; EP 469079 B1 Based on WO 9012579; DE 69014870 E Based on EP 469079, Based on WO 9012579; ES 2064736 T3 Based on EP 469079; JP 08019001 B2 Based on JP 04503813, Based on WO 9012579; US 5792832 A Cont of US 5173408
PRAI US 1989-429398 19891031; US 1989-340868 19890420; US 1994-283723 19940801; US 1989-434899 19891113; US 1992-856910 19920512; US 1994-350801 19941207; US 1995-461881 19950605
REP 2.Jnl.Ref; DE 1492011; GB 1053143; GB 953626; US 3148114; US 4520017; 01Jnl.Ref; GB 1164569; GB 1433732; US 3175942; US 4436731; US 4623539
IC ICM **A61K031-715**; **A61K031-72**; **A61K045-00**; C07K007-06
ICS A23L001-30; A23L001-308; **A61K031-725**; **A61K031-73**; **A61K031-795**; **A61K039-39**; **A61K039-395**; C07K009-00; C12N009-16
ICA C12N009-99

AB WO 9012579 A UPAB: 19991221
Ingestible food prod. contains an effective amt. of a non-absorbable synthetic **cholesterol esterase** inhibitor (I).
Inhibiting the intestinal absorption of **cholesterol** comprises admin. p.o. a non-absorbable inhibitor of **cholesterol esterase** or an antibody directed against **cholesterol esterase**.
Reducing serum **cholesterol** levels comprises admin. of a synthetic non-absorbable **sulphated polysaccharide** in combination with an absorbed **cholesterol** synthesis blocker, triglyceride lipase inhibitor or fatty acyl **cholesterol** O-acyl transferase (**ACAT**) inhibitor.
USE/ADVANTAGE - (I), esp. **sulphonated polysaccharides**, decrease intestinal absorption of **cholesterol** and fatty acid by inhibiting pancreatic **cholesterol esterase**, which is a key enzyme involved in dietary **cholesterol** absorption. (I) are stable and can be incorporated in food prods., including baked prods. for dietary control of serum **cholesterol** levels and atherosclerosis (I) are potent inhibitors; are non-absorbable, so that side-effects are reduced; and are inexpensive. Doses of **cholesterol** synthesis blockers or **ACAT** inhibitors can be reduced, and side-effects minimized, by use with (I).
Dwg.0/10
FS CPI
FA AB
MC CPI: B04-B04C6; B04-B04F; **B04-C02**; B07-A02; B12-G01B2; B12-G01B3; **B12-H03**; B12-J01; D03-H01T
ABEQ US 5017565 A UPAB: 19930928
Method of inhibiting human pancreatic **cholesterol esterase** in the alimentary tract comprises oral admin. of a 3-**sulphated polysaccharide** (I). (I) is pref. 3-**sulphated** alginic acid, pectin, amylopectin, chitin, dextran, cellulose agar or chitosan which are all soluble, potent inhibitors of human pancreatic **cholesterol esterase**.
USE - In inhibiting or decreasing **cholesterol** and fatty acid absorption.
In an example, Na alginate (150 mg) was treated with 5 cc glacial acetic acid for 2 hrs. at room temp., filtered and resuspended in 5 ml N,N-dimethylformamide. To stirred soln. 1.5 g SO3-pyridine complex was added over 30 mins. at room temp. and resulting mixt. stirred overnight for 16 hrs. 5 ml dry pyridine was then added and the **sulphated** alginic acid was pptd. with 10 ml acetone-MeOH (9:1) mixt. before dissolving in 50 ml H2O and adding IN NaOH to adjust pH to 8. Repptn. with 200 ml acetone-MeOH (9:1) mixt. produced the Na salt of **sulphonated** alginic acid. Cpd. was tested for **cholesterol esterase** inhibition and it had IC50 of 0.25 microg/ml or 1.0nM.
ABEQ US 5063210 A UPAB: 19930928
Inhibiting pancreatic **cholesterol esterase** comprises contacting it with a 3-**sulphate polysaccharide** of M.W. 10+ kDa (100+ kDa, 500+ kDa). Pref. the 3-**sulphated polysaccharide** is 3-**sulphated** alginic acid, pectin, amylopectin, chitin, dextran, cellulose, agar or chitosan (Fig.2). Prepn. is e.g. by treating chitosan with glacial HOAc, dissoln.e in DMFA and sulphation with SO3/pyridine.
USE - The method reduces the absorption of **cholesterol** and triglycerides from the intestine and their concns. in the blood stream so reducing risk of atherosclerosis, etc. The material can be eaten in a baked biscuit.
ABEQ EP 469079 B UPAB: 19950117
Use of a non-absorbable inhibitor of **cholesterol esterase** in the manufacture of an ingestible pharmaceutical compostion for inhibiting the intestinal absorption of **cholesterol** wherein said inhibitor is a 3-**sulphated polysaccharide** or an antibody to **cholesterol esterase**.
Dwg.0/7

ABEQ US 5616570 A UPAB: 19970512
A method for inhibiting the intestinal absorption of **cholesterol** in a mammal by administering orally a non-absorbable inhibitor of **cholesterol esterase** comprising a 3-**sulphated polysaccharide** having a molecular weight greater than 100,000 Da.
Dwg.0/7

L232 ANSWER 8 OF 8 WPIX COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1987-039026 [06] WPIX
DNN N1987-029654 DNC C1987-016333
TI Assay of lecithin-**cholesterol acyl-transferase** activity - involves transforming lysolecithin in sample into betaine and hydrogen peroxide and treatment with peroxidase.
DC B04 D16 S03
PA (FUJI-N) FUJIMOTO DIAGNOSTICS
CYC 1
PI JP 61293396 A 19861224 (198706)* 5p
ADT JP 61293396 A JP 1985-135737 19850620
PRAI JP 1985-135737 19850620
IC C12Q001-44; G01N033-92
AB JP 61293396 A UPAB: 19930922
1st Process: Endogenous lysolecithin in sample is transformed to betaine and H2O2 by reaction of lysolecithin-lipase (LYP), glycerophosphoryl choline phospho-diesterase (GPCP) and cholineoxidase (CHO); and produced H2O2, together with N,N-diethyl-m-toluidine and methyl-p-hydroxybenzoate are treated with peroxidase (POD), and decoloured. 2nd Process: Lysolecithin produced by lecithin **cholesterolacyl**-transferase (LCAT) from lecithin and free **cholesterol** as substrate, is transformed to betaine and H2O2 by the same enzyme reaction with 1st process, and by peroxide (POD) reaction, produced H2O2, N,N-diethyl-m-toluidine and 4-amino-antipyrine are oxidatively condensated, and quinoid colour is produced. Absorbence of characteric absorption for the obtd. colour is estimated. In 2nd process, exogenous lecithin is added as substrate, and ester type **cholesterol**, produced with lysolecithin by LCAT reaction is transformed to free **cholesterol** by **cholesterol esterase**.
0/0
FS CPI EPI
FA AB; DCN
MC CPI: B04-B02C2; B04-B02C3; B04-B02C4; B07-D08; B10-B04A; B11-C07B2; B12-K04; D05-A02A; D05-A02B; D05-A02C; D05-H09
EPI: S03-E14H

=> d his

(FILE 'HOME' ENTERED AT 10:59:46 ON 23 JUN 2001)
SET COST OFF

FILE 'REGISTRY' ENTERED AT 10:59:57 ON 23 JUN 2001
E CHOLESTEROL/CN
L1 1 S E3
E CHOLESTEROL ESTERASE/CN
L2 1 S E3
E LOVASTATIN/CN
L3 1 S E3
L4 1 S E5
E C24H36O5/MF
L5 12 S E3 AND C6-C6/ES AND OC5/ES AND 3/NR AND BUTANOIC AND 3 7 DIME
L6 11 S L5 NOT 14C
E C24H38O6/MF
L7 5 S E3 AND C6-C6/ES AND 2/NR AND NAPHTHALENEHEPTANOIC AND 2 6 DIM
L8 4 S L7 NOT 224324-83-8
L9 3 S L8 NOT 101761-41-5
E CHOLESTEROL ACYLTRANSFERASE/CN

```
L10           1 S E3

     FILE 'HCAPLUS' ENTERED AT 11:10:34 ON 23 JUN 2001
L11       73295 S L1
L12        1552 S L2
L13        1355 S CHOLESTEROL ESTERASE
L14          10 S STEROL ESTERASE
L15          81 S CHOLESTERASE
L16         337 S CHOLESTEROL ESTER HYDROLASE
L17         234 S CHOLESTERYL ESTER HYDROLASE
L18          94 S CHOLESTERYL ESTERASE
L19          25 S CHOLESTEROLESTERASE OR CHOLESTERYLESTERASE
L20         113 S LYSOSOMAL ACID LIPASE
L21        2194 S L12-L20
L22        1384 S L3 OR L6 OR L4 OR L9
L23        1988 S LOVASTATIN OR MEVINOLIN OR MONACOLIN# K OR LOVASTATIN ACID
L24          43 S MEVACOR OR MEVINOLINIC ACID
L25        2058 S L22-L24
L26        1482 S L10
L27        3574 S CHOLESTEROLACYLTRANSFERASE OR (CHOLESTEROL OR CHOLESTERYL)()(
L28           3 S STEROL O ()(ACYLTRANSFERASE OR ACYL TRANSFERASE)
L29        1322 S ACYL COA CHOLESTEROL(1W)(ACYLTRANSFERASE OR ACYL TRANSFERASE)
L30           5 S ACYL COA () (CHOLESTEROLACYLTRANSFERASE OR CHOLESTERYLACYLTRA
L31        1078 S ACAT
L32        3968 S L26-L31
L33           8 S L21 AND L25
L34         272 S L21 AND L32
L35           8 S (L11 OR CHOLESTEROL) AND L33
L36           2 S L35 AND ?SACCHARID?
L37           1 S L36 NOT 3/SC
                E HEIDER/AU
L38           1 S HEIDER ?/AU AND 1983/PY AND (24 AND 1127)/SO

     FILE 'REGISTRY' ENTERED AT 11:34:37 ON 23 JUN 2001
L39           1 S 71806-22-9
                E C31H48N2O3/MF
L40           8 S E3 AND NC4-C6/ES
L41           5 S L40 AND TRYPTOPHAN AND ETHYL ESTER
L42           5 S L39,L41
                SEL RN
L43           0 S E1-E5/CRN

     FILE 'HCAPLUS' ENTERED AT 11:37:15 ON 23 JUN 2001
                SET SMARTSELECT ON
L44         SEL L37 1- RN :      13 TERMS
                SET SMARTSELECT OFF

     FILE 'REGISTRY' ENTERED AT 11:37:15 ON 23 JUN 2001
L45          13 S L44
L46           8 S L45 AND S/ELS

     FILE 'HCAPLUS' ENTERED AT 11:37:34 ON 23 JUN 2001
L47           8 S L42
L48           1 S L47 AND L1,L21
L49           3 S L47 AND L25,L32
L50           6 S L47 AND ?CHOLEST?
L51           6 S L48-L50
L52           2 S L47 NOT L51
L53        2795 S L46
                SCA L***
L54        5395 S (CHITIN OR CELLULOSE OR DEXTRAN OR CHITOSAN OR AMYLOPECTIN OR
                E POLYSACCHARIDE/CT
                E E14+ALL
L55         943 S E3,E4 (L) (SULFAT? OR SULPHAT?)
L56      329560 S E3+NT
L57       33516 S L56 AND (?SULFAT? OR ?SULPHAT?)
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L58        6917 S L56 AND (?SULFONAT? OR ?SULPHONAT?)
L59      332085 S L53-L58
L60         162 S L59 AND L25,L32
L61          10 S L60 AND L21
L62           6 S L61 AND (1 OR 63)/SC,SX
L63           3 S L62 NOT (3 OR 6)/SC,SX
L64           2 S L63 NOT HEPATOCYTES/TI
L65           0 S L47 AND L59
                E LANGE L/AU
L66         102 S E3,E6,E18-E20
                E SPILBURG C/AU
L67          37 S E4-E7
                E  REARDAN D/AU
L68          10 S E4-E6
L69          19 S L66-L68 AND L11
L70          24 S L66-L68 AND L21
L71           1 S L66-L68 AND L25
L72           6 S L66-L68 AND L32
L73          14 S L66-L68 AND L59
L74          38 S L69-L73
L75          29 S L74 AND (PY<=1994 OR PRY<=1994 OR AY<=1994)
L76           5 S L75 AND (1 OR 63)/SC,SX
L77           6 S L37,L38,L64,L76
L78           8 S L47-L52
L79           5 S L78 AND (PY<=1994 OR PRY<=1994 OR AY<=1994)
L80           1 S L79 AND L21,L59
L81           8 S L78,L79,L80
                SEL HIT RN

    FILE 'REGISTRY' ENTERED AT 11:58:17 ON 23 JUN 2001
L82           7 S E1-E7

    FILE 'HCAPLUS' ENTERED AT 11:59:05 ON 23 JUN 2001
L83          13 S L37,L77,L81
                SEL HIT RN

    FILE 'REGISTRY' ENTERED AT 12:00:27 ON 23 JUN 2001
L84          27 S E8-E34
L85          40 S L3,L6,L4,L9,L84

    FILE 'REGISTRY' ENTERED AT 12:01:32 ON 23 JUN 2001

    FILE 'HCAPLUS' ENTERED AT 12:03:07 ON 23 JUN 2001

    FILE 'EMBASE' ENTERED AT 12:03:54 ON 23 JUN 2001
L86       44670 S L1
L87       87655 S (CHOLESTEROL BLOOD LEVEL OR CHOLESTEROL METABOLISM+NT OR CHOL
L88      109835 S L86,L87
L89         701 S L2
L90        1049 S L21
L91        1049 S L89,L90
L92         231 S POLYSACCHARIDE SULFATE/CT
L93       64665 S POLYSACCHARIDE+NT/CT
L94        1902 S L46
L95        2944 S L54
L96         153 S ESTERASE INHIBITOR/CT
L97       48421 S ESTERASE INHIBITOR+NT/CT
L98        4191 S L3,L6,L4,L9
L99        4404 S L23 OR L24
L100          6 S L154803 OR L154819 OR L()(154803 OR 154819 OR 154()(803 OR 81
L101          0 S MK819 OR MK 189
                E MEVACOR
L102        371 S E1-E4,E6
L103        984 S L10
L104       2926 S L27-L31
L105        333 S CHOLESTEROL ACYLTRANSFERASE INHIBITOR+NT/CT
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L106          0 S L42
L107        187 S L98-L105 AND L91
L108       5058 S L98-L105 AND L88
L109          0 S L107,L108 AND L92
L110         62 S L107,L108 AND L93
L111          9 S L107,L108 AND L94
L112         20 S L107,L108 AND L95
L113         73 S L107,L108 AND L110-L112
L114         37 S L113 AND PY<=1994
L115          9 S L114 AND (DRUG COMBINATION OR DRUG POTENTIATION)/CT
L116         21 S L114 AND (COADMIN? OR COMEDI? OR COPRESCRI? OR COTHERAP? OR C
L117          9 S L115 AND CB/CT
L118         21 S L115-L117
L119          7 S L118 AND ?SULFAT?
L120          1 S L118 AND ?SULPHAT?
L121          0 S L118 AND ?SULPHONAT?
L122          0 S L118 AND ?SULFONAT?
L123          8 S L119,L120
L124        416 S (MEVINOLIN(L)CB)/CT
L125        684 S MEVINOLIN/CT AND (DRUG POTENTIATION OR DRUG COMBINATION)/CT
L126        684 S L124,L125
L127          0 S L126 AND L92
L128          1 S L126 AND L94
L129          1 S L126 AND L95
L130         12 S L126 AND L93
L131         12 S L128-L130
L132          3 S L105 AND L92-L95
L133          8 S L105 AND L96,L97
L134         11 S L132,L133
L135         13 S L131,L134 AND PY<=1994
L136         10 S L88 AND L135
L137         10 S L136 AND (COADMIN? OR COMEDI? OR COPRESCRI? OR COTHERAP? OR C
L138          4 S L137 NOT AB/FA
L139         12 S L46,L54 AND L104 AND PY<=1994
L140        507 S L46,L54 AND (?SACCHARIDE?(S)(?SULFATE? OR ?SULPHAT? OR ?SULFO
L141        375 S L140 AND PY<=1994
L142         10 S L88 AND L141
L143          9 S L139 AND L88
L144         18 S L142,L143
L145         17 S L144 NOT DEXTRAN (5A) COLUMN
L146         11 S L145 AND ?CHOLESTER?
L147          6 S L145 NOT L146
L148         11 S L86-L145 AND L146

     FILE 'EMBASE' ENTERED AT 12:34:08 ON 23 JUN 2001

     FILE 'MEDLINE' ENTERED AT 12:34:36 ON 23 JUN 2001
L149         84 S ((CHOLESTEROL ESTERASE )(L) AI)/CT
L150     239067 S D9.203.698./CT
L151       1356 S L2 OR L21
L152      71166 S L1 OR CHOLESTEROL/CT
L153      44605 S (HYPERCHOLESTEROLEMIA+NT OR LIPOPROTEINS, HDL+NT OR LIPOPROTE
L154          1 S L42
L155       2924 S L25
                E MEVACOR
L156         33 S E3-E7
                E LOVASTATIN
L157       2840 S E1-E12
L158          3 S E13,E14
                E MEVINOLIN
L159        310 S E3-E8
                E MONACOLIN
L160         22 S E3,E4
L161       1629 S L155-L160 AND L149-L153
L162        995 S L161 AND PY<=1994
L163         89 S L162 AND (DRUG COMBINATIONS+NT OR DRUG THERAPY, COMBINATION+N
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L164          83 S L163 AND LOVASTATIN+NT/CT
L165           9 S L164 NOT AB/FA
                 SEL DN 5-9
L166           5 S E1-E10
L167          74 S L164 NOT L165
L168          74 S L167 AND ANTICHOLESTEREMIC AGENTS+NT/CT
L169          63 S L168 AND HYPERLIPIDEMIA+NT/CT
L170          55 S L168 AND HYPERCHOLESTEROLEMIA+NT/CT
L171          63 S L169,L170
L172          11 S L168 NOT L171
L173          63 S L171 AND ?CHOLEST?
L174        6606 S ?SACCHARID? (L) (?SULFATE? OR ?SULFONATE? OR ?SULPHATE? OR ?S
L175        1201 S L46
L176        2665 S L54
L177        6433 S L174-L176 AND PY<=1994
L178        4682 S L177 AND L149-L153
L179           1 S L178 AND L149
L180           4 S L178 AND L151
L181         277 S L178 AND L153
L182         233 S L178 AND L153/MAJ
L183       21697 S (POLYSACCHARIDES+NT(L)TU)/CT
L184           0 S L183/MAJ AND L182
L185           1 S L183 AND L182

     FILE 'MEDLINE' ENTERED AT 13:12:16 ON 23 JUN 2001

     FILE 'WPIX' ENTERED AT 13:16:05 ON 23 JUN 2001
L186       13404 S ?CHOLESTER?
L187       14771 S P814/M0,M1,M2,M3,M4,M5,M6
L188        9292 S (B12-H03 OR C12-H03 OR B14-D02A2 OR C14-D02A2)/MC
L189       23514 S L186-L188
L190         245 S L23,L24
                 E LOVASTATIN
L191         180 S E1-E6
                 E MEVINOLIN
L192          66 S E1-E6
                 E MONACOLIN
L193          24 S E3,E4
                 E LOVASTATIN/DCN
                 E E3+ALL
L194         164 S E2
                 E MEVACOR
L195           2 S E3
L196         235 S L189 AND L190-L195
L197         216 S L13-L20
L198           1 S L197 AND L196
L199         397 S L27-L31
L200         804 S L54
L201        2601 S L174
                 E CHITIN/DCN
                 E E3+ALL
L202         428 S E2
L203         315 S E4
L204           1 S E6
L205         947 S E8
L206         315 S E10
                 E AMYLOPECTIN/DCN
                 E PECTIN/DCN
                 E E3+ALL
L207         523 S E2
                 E AGAR/DCN
                 E E4+ALL
L208         421 S E2
                 E ALGIN/DCN
                 E E4+ALL
L209        1833 S E2 OR 1866/DRN
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L210        403 S E4
L211          5 S E6
                E DEXTRAN/DCN
                E E5+ALL
L212        193 S E2
L213         46 S E4
L214         11 S E6
L215      31939 S (V71? OR V72? OR V73?)/M0,M1,M2,M3,M3,M4,M5,M6
L216      31846 S (B04-C02? OR C04-C02?)/MC
L217       1574 S L200-L216 AND L189
L218         21 S L217 AND L197
L219          5 S L218 AND A61K/IC

     FILE 'WPIX' ENTERED AT 13:31:15 ON 23 JUN 2001
L220       1044 S L217 AND A61K/IC NOT L218
L221        695 S L220 AND M782/M0,M1,M2,M3,M4,M5,M6
                E A61K031-7/IC
L222        205 S A61K031-7?/IC AND L221
L223         37 S L222 AND (?SULFAT? OR ?SULPHAT? OR ?SULFONAT? OR ?SULPHONAT?)
L224          9 S L223 NOT (FIBROBLAST OR PLASTER OR CARDIOVASCULAR OR ANTACID
L225        183 S L196 AND A61K/IC
L226        183 S L225 NOT L219,L223
L227         92 S L226 AND M782/M0,M1,M2,M3,M4,M5,M6
L228          0 S L227 AND ?ESTERASE?
L229        216 S L13-L20
L230          8 S L199 AND L229
L231          8 S L230 AND L189
L232          8 S L231 AND L186-L230
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